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TREATMENT OF FROSTBITE WITH PARTICULAR REFERENCE TO THE USE OF ADRENOCORTICOTROPHIC HORMONE (ACTH)*

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NEW HAVEN, CONNECTICUT

THE first part of this communication is a detailed presentation of two patients who sustained cold injuries and who were treated with pituitary adrenocorticotrophic hormone. The dosage of the hormone and the duration of treatment were, of necessity, arbitrarily determined. Both patients were admitted to the hospital before thawing of the tissues had progressed beyond the early stages.

METHODS

Studies were made daily during the first few days after admission and at less frequent intervals thereafter. These studies included a detailed examination of the feet, skin-temperature recordings and photographs of the feet. The skin-temperature recordings were made in a constant-temperature room at 76° Fahrenheit. The room temperature did not usually vary more than ± 2°, although variations of ±4° occasionally occurred. The patients were allowed to equilibrate for forty-four minutes, during which time thermocouple leads were attached to a potentiometer (Brown) continuously recording the temperature of the great toes, the dorsa of the feet, both thighs and the forehead. This equilibration time, rather than the more conventional time of sixty minutes, was used because one patient (W. Z.) complained of severe pain, as his feet were beginning to thaw while in the constant temperature room on the day of his admission.

Black-and-white and colored photographs were made of several aspects of the feet of both patients.

CASE REPORTS

CASE 1. W. Z. (G.-N.H.C.H. No. 35-03-31), a 57-year-old restaurant worker, with a history of chronic alcoholism, was admitted on January 5, 1951. He had fallen asleep outdoors in an intoxicated state on the night before admission. He remembered getting his feet wet at some time during the night. On the morning of admission he awoke on the sidewalk with severe burning pain in both feet and was unable to walk. He was brought to the hospital by the police.

About 2 years before admission he had been jailed for alcoholic intoxication. At that time he had been exposed to cold, and while he was in jail his feet became swollen and painful. During his incarceration he was seen at intervals by attending physicians because of pain and swelling of his feet. The symptoms subsided after about 1 month, and he had no further trouble with his feet until the present admission.

On the 1st day (Fig. 1) the great toes of both feet showed moderate pallor. There was also pallor interrupted by spotty

FIGURE 1. *Appearance of the Feet in Case 1 on Admission.*

areas of cyanosis, of the other toes of the right foot. The distal portions of the left 2d and 5th toes were evenly cyanotic, with spotty areas of cyanosis over other areas of both feet. Rubor was apparent on the proximal parts of both feet and on both ankles. There was mild edema of the toes and distal metatarsal region, as well as the proximal portions of the feet and ankles. The patient complained of numbness and severe, burning pain in both feet. There was loss of sensation to light touch and pinprick to the level of the ankles, and marked hyperesthesia on palpation (any pressure greater than light touch) of the toes and dorsal surfaces of both feet. Position sense of the toes was not tested because of the extreme tenderness. The patient was given 12.5 mg. of ACTH every 6 hours.

On the following day pallor had disappeared. The left 5th toe was still cyanotic, and there were a few reddish-blue blotches on the dorsum of the right foot, light pink having replaced all other colors in other areas (Fig. 2). Edema was marked, all toes and both feet and ankles showing great swelling. The veins of the legs above the ankles were swollen (interpreted as indicating a great increase in blood flow to the feet). There was a definite decrease in the sensation of burn-

*From the Department of Surgery, Yale University School of Medicine. Aided in part by a grant from the Medical Fluid Research Fund of the Yale University School of Medicine and supported in part by Contract No. 175 from the Veterans Administration on recommendation of the National Research Council's Committee on Veterans Medical Problems.

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ing pain, loss of sensation to light touch extended to the junction of the proximal and middle thirds of both feet, with bilateral loss of pinprick sensation to the level of the ankles. The hyperesthesia on the dorsal surfaces of the feet was less

FIGURE 2. *Appearance of the Feet in Case 1 on the Second Hospital Day.*

marked than it had been on the previous day. During this 24-hour period the patient received 50 mg. of ACTH.

By the 28th day, examination revealed no cyanosis, although there was still slight swelling of the dorsum of the left foot near the base of the toes (Fig. 3). The patient complained of bouts of coldness and sweating of both feet, with occasional sensations of mild "electric shock" and of moderate aching of the feet while walking (limited to about 100 steps). There was apparently normal perception to light touch throughout both feet, and pinprick sensation was present in

FIGURE 3. *Appearance of the Feet in Case 1 on the Twenty-Eighth Hospital Day.*

all toes. The proximal two thirds of both feet were moist at room temperature (76°F.).

At discharge on the 30th day perception to pinprick was present in the toes and in the distal portions of the feet.

CASE 2. G. C. (G.-N.H.C.H. No. B-74943), a 40-year-old gardener and odd-job worker, was admitted on January 9, 1951. He had spent the 3-day period prior to admission in a heavily intoxicated state about which he remembered only that he spent the entire time in an unheated car on a street near the waterfront. As far as he could recall, he did not get his feet wet. On the morning of admission he was aware that his feet were cold and numb. When he found that feeling did not return to his feet when he stamped and massaged them, he came to the hospital.

Examination on admission disclosed pallor of all toes and of the distal metatarsal region, both plantar and dorsal surfaces. Cyanotic blotching was also observed, but pallor was predominant. There was cyanosis of all surfaces of both feet up to the malleoli plantar and dorsal surfaces, except in the areas of pallor noted above. As the ankles were approached, rubor predominated. The appearance of the plantar surfaces of the feet is presented in Figure 4. There was deep-red discoloration around the ankle region, with minimal

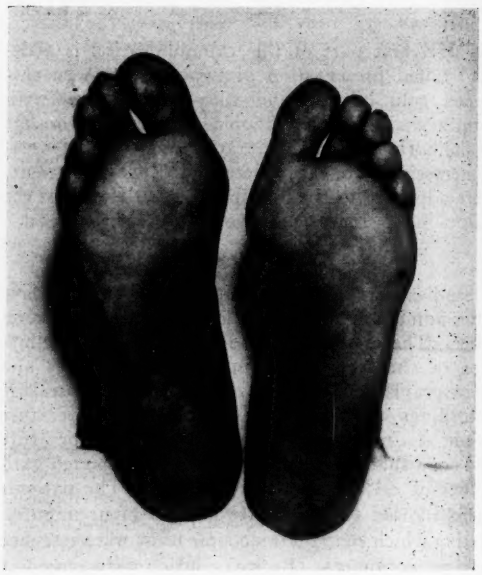

FIGURE 4. *Appearance of the Plantar Surface of the Feet in Case 2 on Admission.*

swelling around the ankles. The patient complained of numbness of both feet (equally) up to the ankles, with a dull ache in the region of the ankles. There was loss of touch and pain sensation involving all toes and the feet to the ankles, as well as loss of position sense in all toes. Therapy on this 1st hospital day consisted of 12.5 mg. of ACTH every 6 hours.

On the 2d day the feet and ankles were no longer cyanotic. The plantar surface of the toes showed nigrescent changes (Fig. 5). The distal plantar skin just proximal to the toes was cyanotic; the right foot disclosed greater involvement of the toes and plantar surfaces than the left. The swelling had greatly increased since admission, all toes and both feet and ankles being involved. There was early blister formation on the dorsal and plantar surfaces of the feet, with minimal blister formation on the great toes. The numbness of the feet and aching of the ankles were still present, and the loss of touch and pain sensation of the toes and feet was unchanged. There was questionable loss of position sense of the toes. ACTH, in doses of 50 mg. per 24 hours, was given.

On the 28th day there was no further progress in the gangrene, and the blackened areas on the soles of the feet were quite superficial and were peeling off (Fig. 6). There was erythema in the horizontal position and very slight edema at

the base of the toes. Symptoms had been minimal for the last few days; the patient occasionally had a dull ache in both feet. Spotty return of pinprick perception in the proximal third of the dorsa of both feet was evident. Touch sensation was present almost to the bases of the toes on the dorsa

FIGURE 5. *Appearance of the Plantar Surface of the Feet in Case 2 on the Second Hospital Day.*

of the feet, but the toes and soles were completely insensitive to touch and pinprick. Position sense was now present in all toes.

Skin-resistance studies revealed no sweating of the soles and distal thirds of the feet. There was sweating of the legs and proximal two thirds of the dorsa of the feet, more marked on the right. A reading of 100 was set with the electrode applied in the grossly perspiring left axilla. The studies were performed after equilibration in a room at a constant temperature of 76°F. for 44 minutes.

One of the patients (G.C.) was exposed for approximately seventy-two hours to an environmental temperature in the range of 47° to 15° Fahrenheit. For at least forty-six hours the temperature was below freezing. He sustained a severe cold injury to both feet. The other patient (W. Z.) was exposed for approximately twelve hours to temperatures in the range of 41° to 26° Fahrenheit, and for over four hours the temperature was below freezing. He sustained a mild cold injury to both feet.

The progressive changes in the feet of these patients after their admission to the hospital and during and after treatment with ACTH are illustrated in the accompanying photographs.

The treatment of these two patients consisted of bed rest, a light, protective gauze dressing (applied with no pressure), sedation as required, penicillin (in one patient), tetanus antitoxin and ACTH. The dose of ACTH in the patient with the lesser injury (W. Z.) was 12.5 mg. every six hours for ten days. In the other patient (G. C.), who had the more severe injury, 12.5 mg. of ACTH was given every six hours for the first 2 hospital days. This dose was then increased to 20 mg. every six hours for the third hospital day and from the fourth to the nineteenth hospital day 25 mg. every six hours. On the nineteenth hospital day the dose was reduced to 12.5 mg. every six hours, and the drug was discontinued on the twenty-first hospital day. In both patients the administration was begun about six hours after admission, after preliminary photographs and constant-temperature-room studies.

RESULTS

In view of the fact that there are no previous reports of patients with cold injury treated with

FIGURE 6. *Appearance of the Plantar Surface of the Feet in Case 2 on the Twenty-eighth Hospital Day.*

ACTH, it is important to review the course of these two cases. Recently Laufman[1] reported on a patient with severe frostbite who received cortisone. Without a control series it is not possible to determine whether or not ACTH influenced the course of the cold injury of these two patients, but it is possible to discuss certain pathologic lesions that ACTH did not prevent. In describing the changes observed in the feet of these patients, the number of days given will represent the actual number of days that the patient was in the hospital, the day of admission being the first.

Edema

The feet of both patients had begun to swell at the time of the first administration of ACTH, and

they continued to swell. ACTH did not prevent the further development of edema or blister formation. Edema began to subside on the third day in W. Z., the patient with the shorter exposure to cold, and on the fourth day in G. C., the patient with the longer exposure to cold. Edema was present to only a minimal degree after the tenth to the twelfth day in both patients. It was of interest that subsidence of edema began at about the same time in both patients and proceeded at about the same rate despite the great difference in the severity of their injuries.

Vasodilatation

Immediately after thawing, the dorsa of the feet of both these patients became warm. Within twenty-four hours or less there was marked vasodilatation of the vessels as evidenced by the very high skin temperatures recorded from the dorsa of the feet at the base of the toes (Fig. 7). It is evident from this graph that vasodilatation persisted in the skin of the feet of G. C. for a prolonged period of time. In W.Z., the patient with the lesser injury, vasodilatation had begun to diminish by the end of the fourth week. The left foot, which was the more severely damaged, was warmer than the right. Since this patient's discharge from the hospital on the thirtieth hospital day, we have not been able to follow him. In G. C., the patient with the more severe injury, a high skin temperature of the dorsa of the feet persisted up to the time of lumbar sympathectomy, ninety-nine days after his admission to the hospital. Skin-resistance studies showed sweating of the feet to be absent on the twenty-second day after admission. By the twenty-eighth day there was gross sweating of the legs, moderate sweating of the proximal two thirds of the dorsa of the feet and no sweating of the distal third of the foot and toes.

Neither of these patients showed a significant rise in body temperature during the administration of ACTH. The highest body temperature recorded during the administration of ACTH in the case of G. C. was 99.6° F., on the second day. The highest body temperature recorded during the administration of ACTH in the case of W. Z. was 99.4°F. on the fourth day.

Subjective Sensation

Both patients complained of numbness of their feet on admission. As the feet began to thaw, and just before ACTH was started, W.Z. complained of extremely severe pain. He was apparently in real agony. By the following morning, approximately eighteen hours after ACTH was begun, his pain was less but still severe. By the third day severe pain had disappeared, but he was aware of occasional sudden "electric-like" shocks that would cause him to wince. Pain at rest in this patient, except for very occasional "shocks," disappeared by the fifteenth day. Aching pain returned in the left foot, however, after he began to walk. The patient, at the time of discharge on the thirtieth day, could walk a moderate distance (100 steps) with minimal discomfort.

The sensation of numbness in the feet of G. C., the patient with the more severe injury, which was present on admission, persisted after thawing until the fourth day. He then began to have intermittent "burning" of the sole of the right foot. This became progressively severe and widespread, involving most of both feet, but by the seventh day the burning sensation had subsided and was replaced by intermittent aching and hot and cold flashes. Numbness was still present in the distal part of the feet and toes. Aching of the feet subsided by the ninth day. "Needle-like" pain in the toes and distal part of the feet began on the tenth day. These sensa-

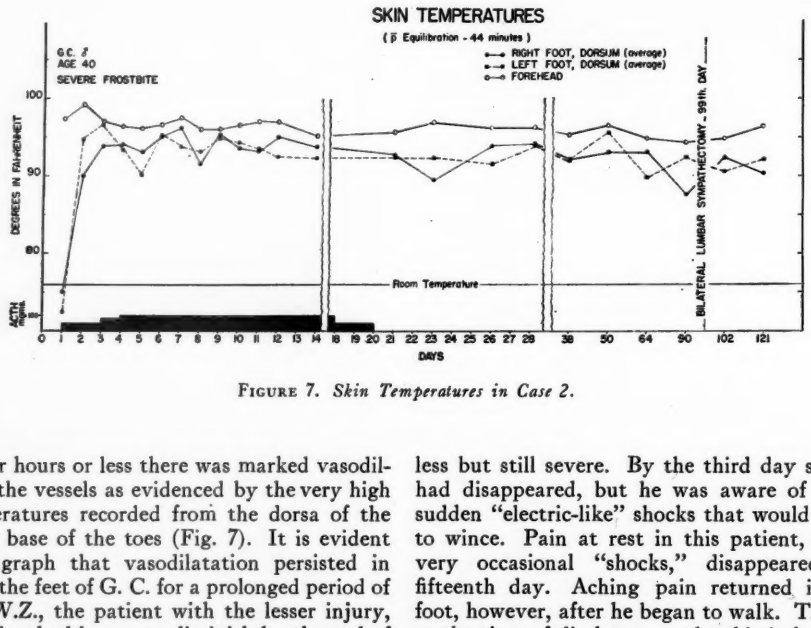
SKIN TEMPERATURES
(½ Equilibration - 44 minutes)
G.C. ♂
AGE 40
SEVERE FROSTBITE
RIGHT FOOT, DORSUM (average)
LEFT FOOT, DORSUM (average)
FOREHEAD
DEGREES IN FAHRENHEIT
100
90
80
ACTH
Room Temperature
BILATERAL LUMBAR SYMPATHECTOMY - 99th. DAY
0 1 2 3 4 5 6 7 8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 38 50 64 90 102 121
DAYS

FIGURE 7. *Skin Temperatures in Case 2.*

tions increased in intensity and were aggravated by the least movement of the toes or feet. He complained also of throbbing in the feet. Exposure of the rest to 68° F. for one hour on the twelfth day apparently resulted in great aggravation of these symptoms. The patient stated that he was able to sleep "only two to three hours at night and not at all during the day" for a period of four days. He refused narcotic medication offered for the relief of pain. By the twenty-first day the pain (which reached a climax between the thirteenth and fifteenth days) had subsided considerably. By the twenty-sixth day he complained only of "throbbing pain" that was intermittent and not severe. Intermittent "shooting pains" continued in both feet until the time of sympathectomy on the ninety-ninth day. After sympathectomy he was temporarily relieved of pain, but after ambulation there was a return of edema and pain in both feet. He was discharged against advice on the 122nd day. He shortly thereafter became intoxicated, walked excessively and was readmitted to the hospital three days later. The feet were swollen, red and very painful. He was discharged to a convalescent home 5 days later.

Objective Sensation

Perception of touch. Loss of perception of light touch was evident in the feet of both patients on admission. This sensation returned over the proximal part of the dorsa of the feet in W.Z. after twenty-four hours. In G. C. touch perception returned on the fourth day over a similar area. In W. Z. this sensation returned to the distal foot and toes on the fifteenth day. In G. C. there was no return of touch sensation to the distal fourth of the feet or toes by the twenty-eighth day, and by the 121st day touch sensation was still absent over the distal 2 cm. of both feet and the stumps of all toes.

Pain. Loss of pain perception as measured by pinprick was evident in both patients on admission. In W. Z. pain to pinprick was experienced in the proximal part of the feet by the fourth day but had not completely returned to the distal part of the feet or toes at the end of four weeks. G. C. showed no return of the sensation of pain to pinprick in either foot to the ankle level by the twenty-third day. There was spotty return of this sensation on the proximal third of both feet by the twenty-sixth day, but there was still no sensation of pain in the distal fourth of the feet or toes by the sixty-fifth day after exposure to cold. By the 121st day there was still incomplete return of pain perception over the proximal half of the dorsal surface of both feet and no perception of pain to pinprick over the remainder of the feet or toes.

Hyperesthesia. In the case of W.Z. this sign was present on the day of admission with any local stimulation greater than light touch (cotton wisp). It began to subside after twenty-four hours and had subsided completely, except for relatively deep palpation, by the seventh day. Hyperesthesia was not observed until the seventh day in G. C., reaching a maximum on the dorsa of the feet on about the thirteenth or fourteenth day and then beginning to subside. By the twenty-sixth day the proximal parts of the dorsa of the feet were only very slightly sensitive to touch, but the distal fourth of the feet and toes, still insensitive to light touch or pain, as yet had not passed through a phase of hyperesthesia. By the 121st day the toes and the most distal part of the feet were still insensitive to touch. The left foot, the less severely injured, showed slightly more recovery of all forms of sensation than did the right foot.

Position sense of toes. This was not tested until the fourth day after injury in W. Z. By this time there was evidence that position sense was present in at least two toes bilaterally. By the seventh day, examination of W. Z. revealed position sense in all toes tested. Position sense of the toes was tested for the first time in G. C. on the second day after injury. The examiner was uncertain whether or not the patient had position perception of the toes on the second or third day. By the fourth day there was definite position perception in the first two toes bilaterally. Return of position sense of the toes was early in both patients — earlier than the return of skin perception to either touch or pain.

Gangrene

Both patients showed areas of cyanosis and pallor on admission.

On admission W. Z. showed spotty cyanosis of both feet. The left second and fifth toes showed evenly distributed cyanosis, involving the distal half of each toe. Twenty-four hours after admission there was cyanosis of only the tip of the plantar surface (site of an old ulcer) of the left fifth toe. At the time of discharge on the thirtieth day there was loss of only the superficial layers of skin over the tip of the left fifth toe.

On admission G. C. showed marked cyanosis of the proximal two thirds of both feet. Pallor, with spotty cyanosis, involved the distal third of both feet and all the toes. Twenty-four hours after admission, cyanosis was confined to the toes, involving the distal phalanx of all toes and in some toes the middle phalanx. In addition, there was cyanosis of a part of the distal plantar surface of both feet, more evident on the right side. Nigrescent changes on the plantar surface of the distal phalanx of all toes began within twenty-four hours after thawing. There was slight but definite progression of nigrescence, especially between the twelfth and twenty-first days, more particularly on the dorsa of the toes. The final lines of demarcation, however, formed within a few millimeters of the areas noted to be cyanotic twenty-four to forty-eight hours after thawing. The final loss of tissue included parts

of all toes, the greatest loss of tissue being in the great toe of the right foot, which was amputated at the line of demarcation through the proximal phalanx.

Comment

From the results of skin-temperature studies of the dorsa of the feet near the base of the toes (Fig. 7), it is obvious that vasodilatation in this region is marked within twenty-four hours after thawing of the tissues begins.* Furthermore, vasodilatation persists for many days. In the patient with the

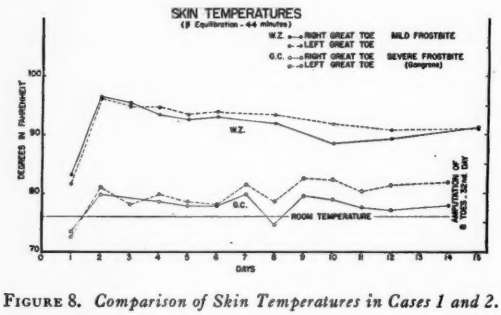

Figure 8. *Comparison of Skin Temperatures in Cases 1 and 2.*

lesser injury (W. Z.), the skin temperature of the dorsa of the feet was slightly lower four weeks after exposure to cold than during the first few days after thawing. In the patient with the more severe injury (G. C.), vasodilatation, as evidenced by a skin temperature of over 90°F. of the dorsa of the feet, persisted for at least ninety-nine days in the right foot. The prolonged vasodilatation in the absence of other signs of inflammation and with the persistence of sensory loss seems to indicate partial or complete paralysis of the vasoconstrictor nerves in the injured area. Because of the high level of the skin temperatures on the dorsa of the feet, a further increase in blood flow could be expected to cause only a moderate additional rise of skin temperature. These findings are in keeping with the experimental results of Fuhrman and Crismon,[2] who found that in tissue surviving cold injury the skin temperature remained high after thawing.

In addition to the five leads placed in series at the base of the toes on the dorsa of the feet, a thermocouple lead was placed at the base of the great toenail on both feet of both patients. Because of blister formation on the dorsa of the great toes of patient G. C., the great-toe leads in this patient were transferred on the third day to the plantar surface of the distal phalanx of the great toes. After the fourteenth day no further skin-temperature recordings were made from the toes of G. C., as the skin on the plantar surface of the toes was obviously gangrenous.

The temperatures of the dorsa of the feet of both patients were in about the same range despite the fact that one patient apparently suffered a much more severe injury than the other. In contrast, as shown in Figure 8, the great-toe temperatures in the two patients were in quite different ranges. The skin of the great toes of patient G. C., which became gangrenous, showed no evidence of vasodilatation but persistently maintained a temperature approximating that of the room. It also should be noted that a low temperature was found on the left great toe of G. C. on the second hospital day when the thermocouple was placed at the base of the nail where blister formation had begun. A low temperature was also found in this patient after the lead on the left great toe had been shifted to the plantar surface of the distal phalanx, the skin of which became gangrenous. In both areas the underlying tissues later proved viable. These findings are in keeping with the experimental findings of Fuhrman and Crismon.[2] They regarded the early fall in skin temperature as a prognostic sign of tissue viability. These authors, confirming the observation of others, found a period of increased blood flow through even the most severely damaged tissue during the first three to five hours after thawing. Within fifty hours after exposure to cold, circulation through the injured tissue ceased and the skin temperature approached that of the room. We did not record the skin temperature of our patients continuously during the first twenty-four hours after admission; hence it is impossible to state whether or not a brief stage of hyperemia developed during this period in the toes of the patient who developed gangrene.

Experimental Studies

The second part of this communication is chiefly concerned with the results of experiments on rabbits' ears, using a standard cold injury in an attempt to evaluate further the influence of ACTH* on the healing of frostbite. In addition some observations were made on the effect of immediate rapid thawing on the healing of experimentally induced frostbite. These experiments will be briefly summarized.

Methods

A standard cold injury was adopted.[3] This consists of exposure of approximately the distal third of the rabbit's ear to a freezing mixture kept between −50° and −60° C. for varying periods of time. In these experiments, exposure for fifteen seconds to ten minutes was used. In the majority the ear was exposed for sixty seconds. With no treatment, the distal third of an ear exposed for fifteen seconds shows a varying loss of tissue from animal to animal, but in general the tissue loss is minimal; after ex-

*Five leads were attached in series (as suggested by Dr. D. L. Brook); thus an average temperature of the five points is recorded.

*Kindly furnished by the Armour Company.

posure for thirty seconds, gangrene is extensive and frequently invoives the entire distal third of the ear; after exposure for sixty seconds or more, total loss of the distal third of the ear almost invariably follows. The progress of the severe cold injury in the rabbit's ear follows a definite pattern,[2] culminating in dry gangrene by the fifth to the seventh day after exposure.

In each group of experiments about half the animals were given ACTH and half were given none. The dose varied from 2.5 mg. to 20 mg. per kg. per twenty-four-hour period, administered intramuscularly in divided doses every six hours. In the majority of the experiments the largest dose was used.

A total of 104 rabbits was used in these experiments. In several experiments both ears of the animals were exposed to the freezing mixture. Fifty-one rabbits received ACTH; 53 rabbits received no ACTH and served as controls. Four groups of experiments were made to determine the influence of ACTH on local tissue response to the cold injury. These were as follows:

Group I. Freezing for sixty to ninety seconds at −50° to −60° C.; thawing at room temperature. There were 8 animals treated with ACTH in this group and 9 controls. Four of the controls died.

Group II. Freezing for thirty seconds at —50° to −60° C.; thawing at room temperature; animals killed after seventy-two hours (20) and after ninety-six hours (20); weighing of the frozen and unfrozen ear of each animal to determine weight-ratio differences in the frozen and normal ears of controls and animals treated with ACTH. There were 40 animals in this group; 20 animals received ACTH and 20 served as controls.

Group III. Freezing at −50° to −60° C. of the distal 4 cm. of ear for thirty to sixty seconds and the immediately proximal 4 cm. of the same ear for fifteen to thirty seconds, respectively; thawing at room temperature. The purpose of this group of experiments was to determine differences in the spread of gangrene from the more severely damaged distal part of the ear to the less severely damaged proximal portion, in animals receiving ACTH and in those receiving no ACTH. There were 18 animals in this group; 9 received ACTH and 9 received none. Both ears of 6 animals in each group were frozen.

Group IV. Freezing for sixty seconds at −50° to −60° C., with immediate rapid thawing for thirty seconds (2 animals — 1 ACTH and 1 control) to one hundred and twenty seconds at +42° C. There were 14 animals treated with ACTH in this group and 15 controls. Two of the animals receiving ACTH and one of the controls died.

Results

The results of these experiments may be briefly summarized as follows:

Group I. ACTH had no influence on the ultimate condition of the frozen tissue in any of these animals. It did appear that dry gangrene developed more rapidly in the majority of rabbits treated with ACTH than in the controls.

Group II. Edema formation in the region of the cold injury appeared to be the same in both the treated and the control animals during the first forty-eight hours following injury. Seventy-two hours after exposure of a measured length of one ear of each rabbit to the freezing mixture, both ears of 20 rabbits (10 treated and 10 controls) were weighed after sacrifice of the animals. The weight of the frozen ear, including a measured length of the unfrozen proximal portion, was compared with a similar amount of the normal contralateral ear. Statistical analysis of the results showed no significant weight difference between the ears of the ACTH-treated animals and those of the controls. However, at this time there was slightly less blister formation and less cyanosis in the ACTH-treated animals. This difference was not observed in the ears of animals with exposure to cold for sixty seconds or more and treated with ACTH. The second group of animals, 10 treated and 10 controls with a similar exposure to cold, were sacrificed at the end of ninety-six hours. Although at ninety-six hours the frozen ears of the control animals were, on the average, slightly heavier than those of the treated animals, statistical analysis again showed no significant difference in the weight of the frozen ears of the treated and control animals.

Group III. There was no appreciable difference in the spread of gangrene to less severely damaged tissue in the ACTH-treated animals as compared with the controls.

Group IV. Immediate rapid thawing resulted in almost 100 per cent salvage of tissue in both treated and untreated animals. There was questionable slight improvement in the final healing of the ACTH-treated animals.

The remarkably beneficial influence of immediate rapid thawing on severely frozen tissues has been studied by a number of investigators.[4-7] We have carried out additional experiments on the ears of 24 rabbits to investigate further this method of treatment. In our studies we found:

In confirmation of the work of Fuhrman and Crismon,[3] gangrene of the distal third of the rabbit's ear usually followed exposure to a temperature of −50° to −60° C. for sixty seconds and immediate rapid thawing in water heated to 42°C. for one hundred and twenty seconds of an ear so frozen invariably resulted in almost total recovery of the frozen tissue. If, however, the frozen tissue was allowed to thaw slowly at room temperature until the temperature of the part had returned to the pre-freezing level (ten to fifteen minutes after removal of the ear from the freezing mixture) and was then

thawed rapidly as above, there was almost *no* salvage of the frozen tissue[6] (Fig. 9).

Mild frostbite (freezing the distal third of the rabbit's ear for fifteen seconds) was not made worse by rapid thawing after slow thawing at room temperature for one hour.

Very severe frostbite (freezing of the distal third of the rabbit's ear for ten minutes) resulted only occasionally, — and then only partially, — in salvage of exposed tissue after immediate rapid thawing. Freezing for one hour followed by immediate rapid thawing resulted in no salvage of tissue. Shumacker and Lempke[8] have also reported less benefit from immediate rapid thawing in very severe cold injuries.

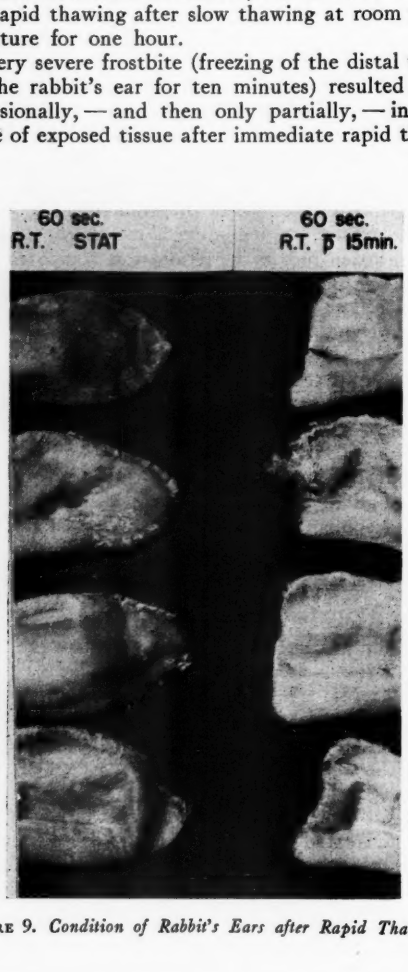

FIGURE 9. *Condition of Rabbit's Ears after Rapid Thawing.*

DISCUSSION

The hope that ACTH might aid the healing of tissues injured by cold was based on the demonstrated ability of this hormone to modify the inflammatory reaction.[9] It was not expected that ACTH would immediately reverse the direct traumatic effect of cold on the tissues, for, although the precise histochemical process involved in the response of tissue to thermal trauma is not clear, the alteration of cell structure is well known, and when the tissues are allowed to return to their normal environmental temperature, cell function will likewise be altered, at least for a time. After thermal trauma directly affects the cell structure and function, capillary permeability is seemingly affected for several days further, possibly through products liberated from the injured cells. Menkin[10] has isolated a substance from a sterile inflammation that will, when injected into normal tissue, cause normal capillaries to become hyperpermeable. Lewis[11] believed that histamine or a histamine-like substance that may cause vasodilatation and hyperpermeability of the capillaries is liberated from cells injured by cold, but this has not been proved.[12] It has recently been demonstrated that ACTH will not neutralize the effect of histamine-like substances liberated from cells after contact with d-tubocurarine.[13]

The inflammatory reaction secondary to thermal trauma is a complex one, and the influence of ACTH on this reaction may be subtle and may only become evident on further study, particularly with relatively mild injuries. On the basis of the two clinical cases studied by us and our experimental work on rabbits, we doubt that the effect of ACTH on the cold injury is of particular therapeutic significance.

It is not the purpose of this paper to review the treatment of frostbite; Shumacker and Lempke[8] have recently published a comprehensive article on this subject. During the course of the studies presented in this report on the patients and animals with frostbite who received ACTH, several observations were made, however, that are pertinent to the treatment of such injuries. One of the most significant findings in the patients studied was the nearly precise relation of cyanosis present twenty-four to forty-eight hours after thawing to the ultimate loss of tissue. This observation was proved by the comparison of color photographs made at frequent intervals. Before thawing, areas of cyanosis were not a reliable guide to the ultimate loss of tissue. Some days after thawing, discoloration of the considerably larger areas of skin occurred, but this was noted over dried-up blisters or involved only the most superficial layers of the skin, under which a complete regeneration of epithelium took place.

The temperature of the exposed part was also of prognostic significance concerning the resultant loss of tissue in the two patients studied. A persistently low skin temperature was noted over the toes that became gangrenous but was also observed over blisters and over areas of skin that became gangrenous but in which the underlying tissues were viable. The temperature of tissues on the distal third of the dorsa of the feet, injured by cold and surviving, was low before thawing but after thawing was excessively high. The vasodilatation in these tissues persisted for many days, even months (Fig.

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7 and 8) and was accompanied by diminished or absent sweating. These findings suggested that, as a result of the cold injury, there was locally, at least in the more distal part of the exposed area, a lack of sympathetic control. Further, a bilateral lumbar sympathectomy (L_3 and L_4), carried out on patient G. C. more than three months after exposure to cold, caused no further elevation in the temperature of the skin over the dorsum of the right foot near the base of the toes. The temperature of the skin over the dorsum of the left foot had begun to fall several weeks prior to sympathectomy, and the operation caused a rise in the skin temperature over the dorsum of this foot. In another patient with frostbite (B. S.) who received no ACTH, a right lumbar sympathectomy was carried out four days after admission and approximately eight days after the onset of swelling of the feet. On admission the right foot showed severe frostbite, with swelling, blistering and cyanosis of all the toes and the plantar surface of the distal half of the foot. The left foot showed swelling and blistering but little discoloration. Sympathectomy caused no further increase in the temperature of the dorsum of the right foot (Fig. 10). After sympathectomy there was a moderate rise in the temperature of the great toe. Nevertheless, gangrene of the great toe developed, necessitating amputation (the other toes of this foot were also amputated).

Denny-Brown and his co-workers,[14] in a series of experiments on animals, exposed the sciatic nerve to cold and found that the sympathetic fibers were the most resistant to cold of all nerve fibers and were destroyed only by very severe exposure. They found in general a direct relation of the intensity of the cold to the degree of nerve injury. Vasodilatation during the early period following thawing, with increased capillary permeability, is probably due, at least in part, to direct injury of the capillary wall by the cold. Persistent vasodilatation for a prolonged period, as evidenced by the increase in skin temperature and the failure to obtain a further rise after ganglionectomy, not accompanied by other signs of inflammation, is probably the result of local paralysis of the sympathetic fibers. The impairment of sensory perception is further objective evidence of nerve damage but, as pointed out by Denny-Brown[14] and Friedman,[15] does not necessarily indicate the degree of damage to the sympathetic fibers.

The effectiveness of sympathectomy in the early treatment of frostbite is difficult to evaluate on the basis of animal experiments. Major difficulties have been the use of different species of animals, different methods of producing sympathetic-nerve paralysis and the great variety of degrees of intensity of exposure to cold. A review of the experimental studies made to date indicates that there is no general agreement concerning the effectiveness of sympathectomy in the prevention of gangrene when it is employed early in the treatment of frostbite. Shumacker[16] has been the chief proponent of sympathectomy in the treatment of frostbite. As yet, the clinical experience with sympathectomy soon after exposure to severe cold is limited. It seems reasonable to expect that sympathectomy performed soon after the injury would cause an increase in blood flow to the injured area provided that the exposure to cold was only mild or moderately severe and the sympathetic fibers had not locally suffered total functional impotence. Some time after the frostbite injury, and presumably after nerve regeneration, painful sequelae develop, usually accompanied by vasospasm. Sympathectomy has been of marked benefit in the relief of these late manifestations of frostbite.[16-18]

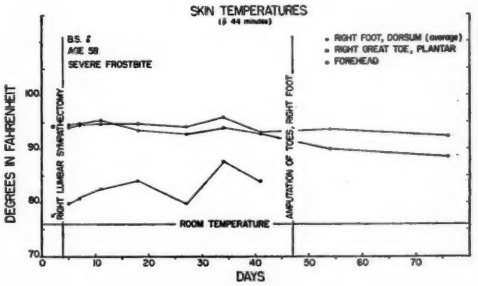

FIGURE 10. *Skin Temperatures after Sympathectomy in a Patient Who Received No ACTH Therapy.*

The remarkable effect of immediate rapid thawing at 42°C. on the survival of frozen tissue in controlled laboratory experiments may be due to several factors.[7] It seems that for rapid thawing to be useful in the treatment of severe frostbite it must take place as soon after exposure as possible, preferably while *all* the exposed part is still cold. It should be borne in mind, however, that in the clinic this method of treatment should be applied with caution and with appreciation of the controlled conditions under which the experimental work has been done.

SUMMARY

ACTH has been used in the treatment of two patients with cold injuries. Since, so far as we are aware, these are the first two cases of frostbite to be treated with ACTH, we have detailed the changes in color, temperature and sensation in the hope that they will serve as a basis for further trial with this hormone and as a means of comparing other methods of treatment when similar observations are made. Although ACTH may have lessened the intensity and duration of some signs and symptoms, it did not cause prompt regression or prevent the development of: increased capillary permeability with

increasing edema formation in the first two to three days after injury; vasodilatation (for prolonged periods); loss of light touch or pain perception; pain; hyperesthesia; or gangrene.

Observations on skin temperature and color changes in the injured area led us to the following conclusions:

Skin that did not eventually become gangrenous showed evidence of vasodilatation with increase in the temperature of the skin.

Skin that did eventually become gangrenous showed no evidence of vasodilatation and tended to assume the temperature of the environment. There may have been a brief period of increased blood flow to tissues that became gangrenous in the early hours after thawing, but this is not shown by the skin-temperature studies made on the first or subsequent hospital days.

A low skin temperature was found over viable epithelium or subcutaneous tissue when these tissues were covered with blisters or nonviable skin.

There was no progressive gangrene of any magnitude, the extent of tissue loss having been determined within forty-eight hours after thawing of the tissue at room temperature (approximately 80°F.). In retrospect, the extent of the loss of tissue could have been predicted, within a few millimeters, from the persistent cyanosis and the presence of low skin temperatures after thawing.

Experiments performed on rabbits' ears revealed that ACTH had no significant therapeutic effect on severe cold injury. Further experiments on rabbits' ears, with immediate rapid thawing, confirmed the findings of others with regard to the efficacy of this method of treatment of cold injury.

Clinical evidence is presented for the complete or nearly complete functional impotence of nerve tissue, including the vasomotor fibers, at least temporarily, in skin seriously injured by cold.

Addendum

We have since treated one patient with cold injury by rapid thawing of the hands and feet in water heated to 110°–120°F. (43.3°-48.8°C.) for three to five minutes, while washing them gently with soap. Superficial blistering of the tips of six fingers developed, but there was no other loss of tissue. The temperature of the tips of the fingers and toes increased after rapid thawing. It was not determined whether this treatment or the mildness of the cold injury was responsible for the favorable outcome.

Acknowledgment

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GLOMERULONEPHRITIS ASSOCIATED WITH ATOPIC DERMATITIS*

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THE constitutional character of atopic dermatitis is generally recognized.[1] The frequent association of this dermatitis with hay fever, asthma and urticaria and the demonstration of specific antibodies by skin tests and passive transfers are sufficient evidence of the allergic nature of the disease. The frequent familial occurrence further establishes the genetic trend to atopic allergy.

On the other hand, allergic mechanisms have also been implicated in the pathogenesis of glomerulonephritis, or at least of certain forms of this disease.[2] In view of this, the simultaneous occurrence of atopic dermatitis and glomerulonephritis might be considered as more than coincidental. In the past two years a number of patients with such an association of the diseases were seen in the Skin Sections of the Veterans Administration Hospitals, Staten Island, New York, and Brooklyn, New York, and a report on these observations seems therefore justifiable, especially since no references to similar occurrences could be found in the literature.

CASE REPORTS

CASE 1 was the first case to call attention to the occurrence of renal disease in atopic dermatitis. A 47-year-old man (Table 1, Case 1) complained of dermatitis and at the same time asthma, which had developed in 1944, at the age of 42. From January to March, 1949, he was hospitalized for severe exacerbation of these diseases, being discharged, greatly improved, on March 25. During this first period of hospitalization, repeated urinalyses were normal. One month after discharge, he was readmitted to the hospital because of considerable deterioration of his condition. He was in a constant asthmatic state, and the dermatitis was almost generalized, very inflammatory and exceedingly pruritic. The face and ankles were highly edematous. There was bilateral pleural effusion. The temperature was elevated, usually around 102 to 103°F. The patient was markedly anemic, with an erythrocyte count of 2,100,000. Between April and August, 1949, the urine consistently contained albumin as well as an appreciable number of granular casts and erythrocytes; repeated concentration tests demonstrated the specific gravity to be no higher than 1.007. The blood urea nitrogen was 32 mg., and the nonprotein-nitrogen 59 mg. per 100 cc. The blood pressure ranged from 144/86 to 158/96. The serum albumin was 2.1 gm. and the globulin 2.9 gm. per 100 cc. The titer of antistreptolysin 0 in the serum was 300 to 400 units. Liver-function tests were normal, as were funduscopic examinations. A skin biopsy presented the picture of chronic dermatitis.

After this case had been observed all subsequent patients with atopic dermatitis were studied carefully for urinary findings and kidney function. As a result, 4 more cases with abnormal urinary findings were found among the 22 succeeding patients. A review of the records of 18 previously hospitalized patients gave evidence of renal involvement in 2 additional cases. Altogether, therefore, a report can be given on 7 well substantiated cases of glomerulonephritis in a series of 41 patients with atopic dermatitis.

Eleven other patients were found to have minimal urinary abnormalities (Table 2). Six of these cases were among the 22 patients studied subsequent to the discovery of Case 1, and 5 others were found in the 18 records of previously hospitalized patients. In all 11 cases the findings were inconstant, consisting only of traces of albumin and sometimes a few granular casts and rare red cells. Usually, not all the findings were present in the same case and at the same time.

The remaining 23 patients with atopic dermatitis had no abnormal urinary findings (Table 2). However, in 11 of these, only one routine urinalysis had

TABLE 1. *Data in 7 Cases of Atopic Dermatitis and Glomerulonephritis.*

CASE NO.	REGISTER NO.	AGE	ADDITIONAL DIAGNOSES	DURATION OF DERMATITIS	URINARY VALUES				
					ALBUMIN (QUALITATIVE)	ALBUMIN (QUANTITATIVE)	GRANULAR CASTS	ERYTHROCYTES	MAXIMUM SPECIFIC GRAVITY
		yr.		*yr.*		*mg./100 cc./day*		*per high-power field*	
1	12658	47	Asthma since 1944	5	++++	810	Present	40–50	1.007
2	2870	39	Infantile eczema; psychopathic personality.	30	++	500	Absent	4–5	1.020
3	4733	38	Asthma	10	++	...	Present	18–20	1.030
4	13839	25	Asthma	20	+++	...	Present	4–5	1.038
5	14092	23	Urticaria; "dermatogenic cataract."	20	+	...	Present	20–30	1.032
6	12195	23	Infantile eczema	20	++++	223	Present	10–20	1.030
7	12321	27	Infantile eczema; nephritis (1938).	6	+	...	Present	5–9	1.030

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been made. The patients had been discharged from the hospital before the first case with renal lesions had been observed, and only their records were available at the time of this study. In the other 12 negative cases repeated urinalyses were normal even when performed twice weekly over periods of at least four to six weeks. Twenty control cases with various nonallergic skin diseases showed no urinary abnormalities on repeated examinations (Table 2).

In the following brief histories of the patients with positive urinary findings Cases 2 through 7 are presented. It should be pointed out in advance that there was no constant correlation between the degree of urinary abnormality and the severity of the dermatitis — for example a rather mild dermatitis was present in Cases 2, 3 and 5. Also, the duration of the atopy and the age of the patient seemed without bearing on the presence, incidence or degree of abnormal urinary findings. Furthermore, in no case except Case 1 were abnormal findings present in all urinalyses performed, and on various occasions the degrees of severity varied. The maximal abnormal values in each case are recorded in Table 1.

Case 2. A 39-year-old woman had suffered from infantile eczema with an additional diagnosis of "psychopathic personality" since 1943. She had had eclampsia in 1942, at 6 months' gestation. Skin tests gave positive reactions to dust, grains and several foods, and there was a possible cold allergy. The dermatitis was moderate but clinically characteristic. Of 8 urinalyses over a period of 7 weeks 3 were negative. There was no parallel between urinary findings and the state of the dermatitis. No casts were ever seen in the urinary sediment, but up to 500 mg. of albumin per day could be found and a maximum of 4 or 5 red cells per high-power field was observed. The specific gravity was normal (1.022), but an abnormal value of nonprotein nitrogen in the serum was obtained (46 mg. per 100 cc.), and there were high values of serum protein and urea nitrogen (Table 1). Kidney function was within normal limits. There was a high diastolic blood pressure. No edemas were noted.

Case 3. A 38-year-old man had suffered from atopic dermatitis and asthma for the past 10 years. Skin tests showed hypersensitivity to dust and ragweed. There were 10 per cent eosinophils among the white cells. The dermatitis was moderate, and responded well to treatment within about 1 month. During this time the initial urinary findings of a ++ test for albumin, occasional granular casts and a maximum of 18 to 20 red cells per high-power field diminished in a series of 5 urinalyses until there were no abnormal findings. A maximum specific gravity of 1.030 was obtained. The patient had maximal blood-pressure values of 140/92, and a slightly dilated, pulsating arteriole was found in the right ocular fundus. Urea nitrogen in the serum was high, but blood proteins and kidney function were within normal range.

Case 4. In this 25-year-old man the dermatitis dated from infancy. Between the ages of 15 and 19 the patient had also suffered from asthma. Multiple hypersensitivities were revealed on skin tests. The peripheral blood showed an eosinophil count as high as 31 per cent. This patient was observed, for several weeks at a time, over a period of 2 years. The dermatitis varied in severity, and there was a clear-cut parallel between clinical course and urinary findings. Between the end of June and the middle of August, 1949, the findings of a +++ test for albumin, granular casts and 4 or 5 red cells per high-power field diminished gradually to normal in a series of 11 urinalyses. The blood urea nitrogen was not higher than 18 mg. per 100 cc., and the serum proteins and urea clearance were normal. There was also a normal specific gravity. However, blood-pressure values as high as 150/90 were obtained.

Case 5. In this 23-year-old man the dermatitis had also started in infancy. However, it had always been rather mild. In the past year a "dermatogenic cataract" of the right eye had developed. Skin tests were positive to nuts, some flowers and dust. Ingestion of nuts caused urticaria. Nine per cent eosinophils were present. Within 1 month 3 of 5 urinalyses were normal, but the remaining 2 urine samples showed up to 20 to 30 red cells per high-power field, occasional casts and a + test for albumin. Blood chemical values, kidney function and blood pressure were normal.

Case 6. A 23-year-old man had infantile eczema, which had become worse since the age of 18. Intracutaneous tests demonstrated hypersensitivity to dust, wool, chocolate and pepper. There was a maximum eosinophil count of 10 per cent. The dermatitis varied from moderate to severe, and a mild pharyngitis developed 2 or 3 weeks after admission. Five or 6 weeks later there was an antistreptolysin titer of 1000 to 1200 per cubic centimeter of serum, and about 3 weeks

Table 1. (*Concluded.*)

Case No.	Blood Chemical Values				Kidney Function		Blood Pressure
	Albumin	Globulin	Urea Nitrogen	Nonprotein Nitrogen	Phenolsulfthalein Excretion	Urea Clearance	
	gm./100 cc.	gm./100 cc.	mg./100 cc.	mg./100 cc.	mg./100 cc.	%	
1	2.1	2.9	32	59	..	..	158/96
2	8.2		15	46	75	..	128/96
3	4.6	2.0	17	..	70	..	140/92
4	4.2	2.2	18	..	..	78	150/90
5	4.8	1.8	14	..	..	..	124/78
6	4.5	2.4	20	40	..	62	140/100
7	..	..	12	..	..	..	160/96

Table 2. *Incidence of Renal Involvement in 41 Cases of Atopic Dermatitis and in 20 Controls.*

Renal Function	Patients with Atopic Dermatitis	Patients with Other Skin Diseases
Renal involvement present	7	..
Suggestive urinary findings	11	..
No urinary findings	23	20
Totals	41	20

later the titer was 1200 to 1400 units. No abnormal urinary findings were present on admission but 1 or 2 weeks after the pharyngitis a trace of albumin, occasional granular casts and 2 or 3 red cells per high-power field were observed. In the next 2 months, 20 urine specimens were examined, 16 of which gave positive findings of a maximum of ++++ test for albumin (223 mg. per 100 cc. per day), usually 3 to 5 granular casts and a maximum of 10 to 20 erythrocytes per high-power field. However, there was a gradual decrease of these findings to normal, and this tendency coincided with the improvement of the dermatitis even at a time when the antistreptolysin titer was rising. During all this time blood chemical values, kidney function and specific gravity remained essentially normal except for the serum nonprotein nitrogen, which was somewhat high (40 mg. per 100 cc.) and one blood urea nitrogen finding of 20 mg. per 100 cc. The blood pressure at one time was found to be 140/100 but was usually measured about 110/70.

Case 7. This 27-year-old man had had eczema as a child, but the atopic dermatitis had first started 6 years prior to admission to the hospital. He had, however, a history of nephritis in 1938, at the age of 16. He was hypersensitive to at least 17 different types of "miscellaneous" allergens and foods. There were 19 per cent eosinophils in the peripheral blood. A series of urinalyses revealed constantly some abnormal findings, usually either red cells or casts or albuminuria. However, the specific gravity of the urine was normal, as was the blood urea nitrogen. Total blood cholesterol values did not go higher than 206 mg. per 100 cc. (no edemas were apparent). The blood pressure was relatively high, up to 160/96, and there were signs of probable myocardial damage in the electrocardiogram.

Discussion

The presence of glomerulonephritis in 7 of 41 patients with atopic dermatitis suggested a more than coincidental association of the two diseases. The fact that minimal urinary abnormalities were found in 11 additional patients and that only one urinalysis had been made in 11 of the 41 patients points to a possibly higher incidence of renal lesions in atopic dermatitis. However, since the total number of cases studied was still rather small, no statistical evaluation is attempted, and the possible significance of the figures mentioned cannot be emphasized at present.

Nevertheless, it should be pointed out that a control group of 20 patients with various skin diseases of differing severity and extent revealed no urinary abnormalities on repeated examinations (Table 2). The analyses in these cases were made in the same laboratories, by the same personnel and at about the same time as the tests in the urine-positive cases of atopic dermatitis. The negative findings in the control group suggest at least some significance of the occurrence of glomerulonephritis in cases of atopic dermatitis.

To permit more positive evidence in favor of a pathogenetic relation between glomerulonephritis and atopic dermatitis there should first be ruled out any possible causes of glomerulonephritis in skin diseases, other than atopy or allergy. The therapeutic use of potentially nephrotoxic substances must be mentioned as one of these causes. In this respect, no correlation could be found between topical applications of tars and similar substances and positive urinary findings. In Cases 1, 3, 4 and 5 albuminuria was present although no tar ointments had been used, whereas in another (Case 1) there was no albuminuria at the time of the first hospitalization despite the use of coal-tar ointment and modified Wilkinson's ointment (with 20 per cent oil of birch tar).

The most frequent cause of glomerulonephritis is, of course, a systemic infection, usually with streptococci. Such an infection might have been present, as a sequel of pharyngitis, in Case 6; yet the subsidence of the nephritis in this case simultaneously with the improvement of the dermatitis, and at a time when the antistreptolysin titers were still rising, could be considered as evidence for the relation of the nephritis to the dermatitis, and against an infectious cause. No history of infections was elicited in any of the other cases. Nevertheless, in Case 7, the nature of the nephritis was such that an infectious etiology could not be entirely ruled out. Generally, however, it seems permissible to exclude infections as a cause of the nephritides in at least 6 of the 7 cases.

Of other systemic diseases producing renal lesions only eclampsia could be considered as far as this series of patients is concerned. This condition occurred in Case 2 only after many years of atopic dermatitis, and the nephritis could therefore have preceded the pregnancy. Furthermore, persistent nephritis five years after eclampsia is very rare and therefore improbable.

Against all this negative evidence a number of positive arguments strongly favor the concept of a pathogenetic relation between glomerulonephritis and atopic dermatitis. Foremost among these is the parallel course of the two diseases in Cases 1, 3, 4 and 6. The details of the urinary abnormalities, as compared with the state of the dermatitis at a given time, were described sufficiently to show the parallel between nephritis and dermatitis in these cases. The presence of normal urine prior to exacerbation of skin lesions, especially in Case 1, is particularly strong evidence in this regard. It might also be mentioned that in Cases 2 and 5 insufficient urinalyses were performed to justify conclusions regarding a possible relation between the severity of the dermatitis and the glomerulonephritis, and that these 2 cases could conceivably also have shown a more or less clear-cut parallel between the two diseases if a greater number of urinalyses had been performed.

A further argument in favor of the atopic character of the nephritis is the occurrence of allergic nephritides observed in rare cases of serum sickness[3] and urticaria,[4] as well as after therapeutic use of rhus toxin.[5] In animals, allergic glomerulonephritis was experimentally produced through the injection of antigenic serums.[6-11] Nephritides in collagen diseases also appear to be of a similar, noninfectious allergic character, as shown by the experimental production of periarteritis nodosa.[12]

Allergic kidney disease is probably present not only in atopies and collagen diseases but also in certain hypersensitivity states, as in rhus dermatitis,[13] after a contact type of dermatitis due to an insect repellent,[14] after bee sting[15] and in secondary syphilis.[16] Although the renal lesions in these diseases are not those of glomerulonephritis but of nephrosis, their existence tends to confirm the possibility of allergic types of kidney diseases. In this connection mention must be made of a case reported in the literature in which a recurrent nephrosis was found in a person who suffered from atopic dermatitis.[17]

In view of all these considerations the described cases of glomerulonephritis might be interpreted as atopic. The development of such atopic nephritides could be conceived as indicating a spread of the allergy to involve more than one shock organ, an occurrence that is actually quite characteristic of atopies. From this point of view it could be postulated that in rare cases there would occur generalizations of the atopic hypersensitivity, which would then produce clinical pictures and laboratory findings similar to those present in Case 1 of this series. In this case the disease had a striking similarity to periarteritis nodosa, and this diagnosis had even been considered by several observers but no vascular lesions could be found in the skin biopsy; however, the unique character of the disease still seems to suggest a certain relation to the extreme hypersensitivity state of periarteritis nodosa.

For the present one may accept Fishberg's[2] statement that "the role of allergic mechanisms in the pathogenesis of glomerulonephritis offers a fruitful field for further investigation."

Summary

Glomerulonephritis, manifested by albuminuria, casts and hematuria, was found in 7 of 41 cases of atopic dermatitis. In 4 of these cases the course of the nephritis was parallel to that of the dermatitis. Otherwise, there was no constant correlation between urinary findings and severity of the dermatitis.

In 11 additional cases minimal urinary abnormalities were found.

Development of the nephritides from potentially nephrotoxic substances could be excluded. Infections and other nonatopic factors were absent in 6 of the 7 patients. In 1 case the similarity of the clinical picture with periarteritis nodosa was particularly suggestive of a hypersensitivity character of the nephritis.

The occurrence of various types of allergic nephritides and nephroses, reported in the literature, is mentioned as supportive evidence for the atopic concept of glomerulonephritis in atopic dermatitis.

Addendum

Follow-up studies on Case 1 over a period of thirty-eight months (until March, 1952) showed repeatedly the same pattern of regular association of dermatitis, asthma and nephritis in several exacerbations of the atopic disease. There were no further episodes of serous effusions, arthritis, anemia or fever, but especially in the fall and winter of 1951–52, there were several severe exacerbations of the dermatitis-asthma complex that were regularly accompanied by the development of urinary findings characteristic for glomerulonephritis. Blood pressure, eye grounds and blood chemical values did not change appreciably. Cortone and ACTH had a beneficial effect on all phases of the disease. At present, the patient is in excellent condition, and there are no abnormal urinary findings.

Case 4 was seen over a period of about two years, and he was finally discharged from active therapy at a time of complete remission, both of the clinical signs and symptoms and of the abnormal laboratory findings.

Case 5 was seen on follow-up examination about five months after hospitalization, when he was found free of active skin lesions, showing only mild lichenifications. A urinanalysis performed at that time revealed "rare red cells" in the sediment but no albumin or casts.

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THE PREVENTION OF THROMBOEMBOLISM IN ACUTE CORONARY-ARTERY DISEASE*

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PRESENT treatment of coronary thrombosis includes, almost without fail, some prophylactic measure intended to prevent thromboembolic complications. This normally consists of one of the coumarin derivatives, heparin or a combination of these drugs. By these methods mortality has been cut approximately by half and thromboembolism to at least an equal degree.[1-3] The inescapable conclusions are that all such patients should receive anticoagulants. An occasional report, however, suggests that not all victims of myocardial infarction need be so treated. Russek and his coworkers,[4] for example, believe that it is possible to select the dangerously ill patients with a predictably high incidence of complications for treatment with anticoagulants. On the other hand, the good-risk patients normally have such a low mortality that the risk of hemorrhagic complications from anticoagulants may be in excess of the preventable mortality.

In a recent report from this hospital involving 207 consecutive cases of acute coronary-artery injury an impressively low incidence of thromboembolic phenomena was noted.[5] This, at first, was attributed to the successful use of anticoagulants. The conclusion appeared less warranted, however, in view of the fact that many of the cases were, by present standards, inadequately controlled, and that one group of 25 patients (who formed the basis for another study) received no anticoagulants. It was also apparent, as suggested by Russek et al.,[4] that serious complications occurred in the patients who were sickest at the outset. The good-risk patients continued to do well almost without exception.

As a result of these studies, methods of treatment were re-examined, and the following plan instituted. Only the very ill or poor-risk patients were to be treated with anticoagulants. The criteria were as follows: age over sixty; history of prior myocardial infarction; findings of congestive failure; persistent shock; intractable pain or high fever; history of prior thromboembolism; auricular fibrillation; peripheral vascular disease; and findings of venous inflammation or thrombosis.

Decision regarding the use of anticoagulants was to be made as soon as possible after admission. Heparin, in sufficient quantities, and Dicumarol were to be administered simultaneously, and the former omitted when prothrombin activity was reduced to 20 per cent of normal. Dicumarol was to be continued in adequate dosage to maintain a level of 15 to 20 per cent until the patient was well ambulated. Anticoagulants were not to be employed in any patient with a history of peptic ulcer, severe hepatic disease or bleeding tendency. All the others, the less seriously ill, and the good-risk patients were to receive no anticoagulants but were otherwise to be treated in the same fashion.

Other, nonmedicinal prophylactic measures were, however, to be employed in all cases: These were to consist of the following:

Limited sedation — it is not considered necessary or even desirable to remove every vestige of pain during the first few hours if this necessitates heavy narcosis.

Encouragement of activity in bed, moving from side to side, frequent leg exercises and self-help, including shaving, washing and feeding.

Elevation of the head of the bed on 10-inch blocks and use of a footboard.* (This somewhat uncomfortable position causes the patient to slide down toward the foot of the bed and encourages frequent change of position largely involving the leg muscles; the bed is kept unbroken at hips and knees, and pillows behind the knees are forbidden.)

Light massage of the legs during bed bath and back rub.

Use of the toilet — this is permitted from the first day in all except the extremely ill patients.

Early ambulation — an occasional patient, as soon as he is free of pain, is allowed limited ambulation† including bathroom privileges, sitting in a chair and walking around the bed. (To be sure, this is not practiced in patients who have no pain but who have other evidence of extensive disease, but some patients, particularly the very obese, are allowed to sit up most of the day or even at night if more comfortable in this position; in most of those actually confined to bed, ambulation is begun at the end of the second week and occasionally as early as the tenth day, and with rare exceptions all patients are walking by the third week.)

RESULTS

During the eighteen-month period between September, 1950, and March, 1952, 169 consecutive patients with acute coronary-artery disease were treated at the West Roxbury Veterans Adminis-

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*This maneuver was first employed by Dr. Robert R. Linton as a prophylactic measure in postoperative patients.

†Seven patients of the group studied were never confined to bed during the day.

tration Hospital according to the plan outlined above.* The group included 123 cases of classic myocardial infarction, 25 of subendocardial infarction, 21 of atypical, lesser infarctions and cases of coronary failure. The average age was fifty-three and four-tenths years; the peak incidence was at fifty-eight years. There were 25 deaths, a mortality of 14.8 per cent. This rather low figure may have been due in part to the fact that no women were included. In women the mortality from acute myocardial infarction is said to be 50 per cent greater than in men.[6] Included among the fatal cases were 2 patients who died within an hour of admission, 2 who failed to survive for eight hours, 2 who died within twelve hours, 4 who died within twenty-four hours and 3 more who died within forty-eight hours. In each of these cases the gravity of the situation was apparent on admission. Some of these patients received anticoagulants and others did not. In some cases there was no time to institute such therapy, and in others all efforts were directed to maintenance of circulation and blood pressure or the correction of serious arrhythmias. All but 1 of these patients were examined post mortem, and showed no thromboembolic disease. All died as a result of extensive infarction. It is apparent that the use or nonuse of anticoagulants played no part in the outcome. These cases are therefore not further considered in this study.

Of the 156 patients who survived for forty-eight hours, anticoagulants were employed in 44 and not given in 112. Included among the nontreated patients were 5 who received anticoagulants for brief and insufficient periods and in whom the drug was stopped for various reasons. There were 7 deaths among the treated cases, a mortality of 15.9 per cent. Six of the deaths occurred in very seriously ill patients, and the outcome was predictable. The other patient, however, was not extensively prostrated on admission but was given anticoagulants because he was over sixty years of age. He died on the fourth hospital day of a cerebral hemorrhage, which resulted, apparently, from the anticoagulant used. None of the 5 patients showed thromboembolism at autopsy.

There were 5 deaths among the 112 patients not protected by anticoagulant drugs, a mortality of 4.4 per cent. One of these, a patient who died suddenly on the fourth hospital day, should have received Dicumarol according to the established criteria; death in his case was due to an extensive myocardial infarction, there being no evidence post mortem of venous thrombosis, pulmonary infarction or embolism. One other patient who was desperately ill experienced the myocardial infarction during the course of an extensive gastrointestinal hemorrhage. Anticoagulants were not administered, for obvious reasons. He died on the fourth hospital day of a ruptured ventricle. A third patient of this group was admitted after five days in another hospital, where unsuccessful attempts had been made to control paroxysmal ventricular tachycardia. This patient was critically ill when first seen, and his condition continued to deteriorate, with congestive failure, vascular collapse and persistent ventricular tachycardia. Anticoagulants were deferred while attempts were directed at correction of more pressing symptoms. He died three days after admission. Post-mortem examination failed to reveal any thromboembolic phenomena in this case. Only 2 of the 5 fatal cases could have been classified as good-risk patients. Both patients died suddenly, one on the fifth and the other on the eleventh hospital day. No autopsy was possible in 1 case. In the other there was no evidence of thromboembolism post mortem.

*Not included are 3 patients who were being treated for chronic congestive heart failure, together with other complicating conditions, in whom autopsy showed terminal coronary thrombosis.

Pulmonary Infarction

In the surviving patients a clinical diagnosis of pulmonary infarction was made in 6 cases — an incidence of 4.2 per cent. The infarction occurred in 4 patients receiving anticoagulants and in 2 who did not. One of these was a poor-risk patient in whom anticoagulants were contraindicated because of a history of peptic ulcer. The other infarction occurred in a relatively young man who was, apparently, experiencing a benign convalescence. However, he exhibited extreme apathy and was far less active than was considered desirable. Such an attitude, if it results in unusual physical immobility, should probably be considered an indication for anticoagulant prophylaxis.

Other Thromboembolic Complications

There were 9 other embolic or thrombotic accidents. These included arterial emboli to the legs in 2 patients, 1 of whom was receiving Dicumarol. There were 7 cerebrovascular accidents. Most of these were probably embolic and occurred in 5 patients on anticoagulants and in 2 not receiving the drug.

Further Observations

As the study progressed it became apparent that the indications for anticoagulant prophylaxis were more numerous than was necessary. Age, apparently, was an unimportant index except that myocardial infarctions are more commonly severe in the aged. However, when the findings of serious injury were lacking the elderly patients were found to do as well as the younger ones. Similarly, patients with a history of prior myocardial infarction were frequently much more seriously ill than those experiencing their first injuries and exhibited a higher mortality. When there was no failure or shock, however, they progressed satisfactorily and experienced no more complications than the other good-risk patients. The presence of peripheral

vascular disease did not appear to influence the course of the illness. Arrhythmias per se were found to be relatively unimportant. Similarly, the presence of bundle-branch block in an otherwise good-risk patient seemed not to influence the course. Accordingly, isolated findings of advanced age, history of prior myocardial infarction, peripheral vascular disease, auricular fibrillation and bundle-branch block, when unaccompanied by other evidence of extensive disease, are no longer considered indications for anticoagulant prophylaxis.

It became apparent that the initial clinical appearance of the patient constituted the best index to his future course and the deciding factor regarding the use of anticoagulants. More specificially, this related to the presence or absence of congestive failure, persistent shock, high fever or intractable pain. Currently, the presence of any or all of these findings is considered an indication for anticoagulant prophylaxis. Inflammatory or thrombotic venous disease during the course of myocardial infarction requires anticoagulant therapy. In addition, it is believed that a history of prior thromboembolism may be another indication. Lesser but probably important indications are the presence of gross obesity, immobility and mental depression or apathy.

Discussion

The importance of thromboembolic complications during the course of myocardial infarction is, today, universally recognized. The best manner of prevention, however, has not been completely determined. Anticoagulants in current use are undoubtedly efficacious in the prevention and treatment of intravascular clotting. Still, it would be premature to conclude that this is the only method, or even the best means, of limiting the incidence of thromboembolism. Most observers are in agreement that the source of most complicating venous thrombosis is in the veins of the legs and that the immediate cause for this phenomenon is stasis.[7, 8] When complete immobilization is practiced or when movement is impossible, drugs that inhibit clotting are obviously indicated. On the other hand, when free movement is permitted, stasis is prevented and thrombosis does not, apparently, occur with any significant frequency.

Though much has been written on the subject, there is no clear evidence at present that early ambulation has any adverse effect on the healing of myocardial infarction. It is common experience to encounter patients with unmistakable evidence of myocardial infarction who never interrupted their normal activities. Other patients are seen on the seventh or eighth day of the illness who spent their most critical first days at work or business. Such patients are obviously the mild, good-risk types, and do well. Conversely, long confinement to bed requires unduly extended convalescence and often initiates profound neuroses. Our own observations indicate that considerable movement in bed, mild activity and early ambulation have no deleterious effects on convalescents from myocardial infarction. This is in accord with the views of Irvin and Burgess,[9] who conclude that ambulation can be begun two weeks after myocardial infarction in most cases. Early ambulation not only did not increase morbidity but was distinctly beneficial. In the group of patients under consideration, no exaggerated incidence of extension of coronary thrombosis or of rupture of the myocardium attended the shortened convalescence. If, as indicated in this report, early ambulation together with free movement in bed also serves to prevent thromboembolism, it should, when possible, be the method of choice.

The suggested aids to encourage free movement, together with avoidance of oversedation and of measures that make for too much comfort in bed, are deemed to be of considerable value. Probably other means or devices will be advanced as further experience is gained in the more active treatment of acute coronary-artery disease. The use of elastic stockings, for instance, is a measure that merits further trial.[10] This method speeds the flow of venous blood by reducing the caliber of the leg veins.

There is no strong evidence that anticoagulant drugs influence in any degree the development of mural thrombi over the sites of myocardial infarctions or the systemic emboli that may ensue. Such accidents occurred in greater numbers among the treated patients of this series, probably because they had more extensive infarctions and associated mural thrombosis.

Anticoagulant prophylaxis is not a completely harmless procedure as has now been reported on a number of occasions.[11, 12] One death in this series was attributed to the adverse effects of the drug. There were also several less serious complications. One patient who was not on anticoagulant therapy experienced a massive hemorrhage from an unsuspected duodenal ulcer on the fourth day of his illness. It was severe enough to require transfusion. He recovered from both conditions. Though the outcome could not have been predicted, it appears likely that this patient might have been less fortunate if the prothrombin activity had been suppressed to therapeutic levels.

The added expense to a patient undergoing anticoagulant treatment is not inconsiderable. The cost of drugs and laboratory studies is estimated to be about $100 in the average case. Though not of primary concern, this sum, particularly when multiplied many times, as in hospital practice, can assume important proportions.

It has been suggested that the mortality of myocardial infarction and the incidence of complica-

tions are lower in some hospitals because fewer extremely ill patients are admitted.[8] A similar criticism could be directed at this report though its validity might be questioned in view of the large number of patients who died within a few hours of admission. In any event, no attempt is being made to discredit the efficacy of anticoagulants or to minimize the need for their employment in properly selected patients. Attention is called, however, to simpler and entirely effective methods for preventing thromboembolic phenomena in the large proportion of patients with acute coronary-artery disease in whom a low incidence of complications and low fatality rate is expected. In this group the hemorrhagic dangers of anticoagulation approach or exceed that of the primary disease.

In this series 112 (71.8 per cent) of the 156 patients who survived for forty-eight hours were treated without benefit of anticoagulants. With the present, more limited criteria 122, or 78.2 per cent, would not have received heparin or Dicumarol. It is believed, therefore, that only 1 out of 4 average hospital patients with acute myocardial infarction falls into the class requiring medicinal prophylaxis for thromboembolism.

Summary and Conclusions

Recent doubts regarding the necessity for anticoagulant treatment in acute myocardial infarction led to a study in which these drugs were employed only in patients with evidence of extensive myocardial injury. These patients were deeply prostrated, and prolonged hospitalization was anticipated. The remainder received no anticoagulants. All were encouraged to move freely about in bed and to feed, wash and shave themselves. Ambulation was practiced early, in the large majority between two and three weeks. The mortality in the patients not receiving anticoagulants was 4.2 per cent. This included 3 extremely ill patients in whom anticoagulants were contraindicated or omitted for other reasons. Better selection would have reduced the mortality to 1.8 per cent. In no case was pulmonary infarction found at autopsy. Clinical, nonfatal pulmonary infarction occurred twice in this group. The patients who received anticoagulants and who were also sicker had not only a greater mortality but also a higher incidence of thromboembolic complications.

It is concluded, therefore, that anticoagulant therapy should be reserved for the patients with acute myocardial infarction who show evidence of extensive disease such as congestive failure, prolonged shock, intractable pain or high fever and may be expected, if they recover, to be confined to bed for a long time. Such cases constitute no more than 25 per cent of average hospital patients with acute coronary-artery disease. All other patients with acute myocardial infarction receive adequate protection from thromboembolism if they move about freely in bed, are not allowed to lie quietly for long periods and are ambulated early.

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MEDICAL PROGRESS

MENTAL-HEALTH ASPECTS OF CIVIL DEFENSE

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CIVIL defense as now known has been in existence about five years. Officials responsible for working out the various programs on the national, state and local levels meet with a wide variety of responses from the citizens they are trying to protect, ranging from infrequent enthusiastic co-operation to more general apathy and occasional outright opposition. The eventual development of civil-defense organization and plans adequate to function in case of dire emergency is extremely difficult but equally necessary.

Because of the present uncertain times, the war that is neither hot nor cold, the tense, almost malignant, way of criticizing officials who try to serve honestly and the complacency toward those who exhibit varying degrees of unethical behavior, the American people are deeply disturbed. The values and ideals that have appeared to work and make sense in the past on a personal and local scale do not seem applicable at national and world levels. Communication is mechanically excellent, but the wrong ideas spread as rapidly as the good. Fear and anxiety fluctuate apparently without rhyme or reason. Some fears are magnified; others more serious may be ignored. Scapegoats, rightly or wrongly, are singled out for blame for all that goes wrong. In a setting that is potentially so full of dangers for undesirable mass action, measures to prevent panic during emergencies and to build morale need to go hand in hand with plans for physical protection.

Drayer[1] has pointed out a glaring paradox in the relation of military and civil-defense planning. Either too much for military defense or not enough for civilian defense is being spent. He believes that civilian defense as now conceived will not be of much help in a severe emergency such as an atomic-bomb attack. He thinks that the whole fundamental philosophy on which present plans are constructed should be challenged. Civilian defense, in his opinion, should be either made effective or abandoned if the nation is not to be lulled into a false sense of security. He goes so far as to suggest that some form of conscription may be necessary in the great metropolitan and industrial centers if any program is to be made effective. He thinks that people should realize that in the event of atomic disaster hardships will be far beyond any they have ever experienced before. He believes that the attitude of "blood, sweat and tears" is the soundest in this area.

Because of the fact that relatively few civil disasters have occurred in the United States, any preparation for large-scale misfortunes in the future must be based on reasoning by analogy with experience in relatively minor disasters. In addition, the experiences of bombed populations in England, Germany and Japan may be helpful in such planning. In any case, a review of some of the commonly held views of group behavior under stress may be useful.

GROUP BEHAVIOR UNDER STRESS

The individual reacts to fear by mobilizing his physiologic energies for fight or flight.[2] His heart rate speeds up, his muscles stiffen, his skin becomes pale, and within his body various chemical and hormonal changes occur as a reaction to this stress that seems designed to help him to fight more vigorously or run faster than he would otherwise be able to do. When so stimulated by fear he may or may not use the best judgment of which he is capable when not so stimulated. When in a group, however, men and women react in part as individuals, but in addition there is an added circumstance that may move the group to incredibly foolish action or to unbelievable heights of heroism. Which way the group will go depends on many factors — its previous individual experience, its conditioning, its reason for existence and, above all, its leadership.

What is the chief difference between the individual and the group? Observations of the French sociologist Le Bon, summarized by Freud,[3] throw some light on this question. He states that in a group the individual is brought under conditions that allow him to throw off the repressions of his unconscious instincts. In a sense the conscience disappears. The individual develops a sentiment of invincible power that allows him to give free rein to instincts, which, had he been alone, he would have kept under control. He feels anonymous and in consequence irresponsible, and hence the sentiment of responsibility that usually controls individuals disappears entirely. Attitudes in a group become contagious. The individual readily sacrifices his personal interest to the collective interest. The cultivated person in such a crowd becomes a barbarian, his actions determined by his instincts. Le Bon[4] expresses this reaction as follows:

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> A group is impulsive, changeable and irritable. It is led almost exclusively by the unconscious. The impulses which a group obeys may according to circumstances be generous or cruel, heroic or cowardly, but they are always so impervious that no personal interest, not even that of self-preservation, can make itself felt. Nothing about it is premeditated. . . .A group is extraordinarily credulous and open to influence, it has no critical faculty. . . .the feelings of a group are always very simple and very exaggerated.

To continue with LeBon's ideas, the group is excited by any excessive stimulus. Extremes are usual. Logic is unnecessary. Anyone wishing to influence the group must do so forcibly with exaggeration and with much repetition. Groups not only may not display a falling away of individual inhibitions and the appearance of cruel, brutal and destructive instincts that are stirred up to find free gratification, but also are capable of great unselfishness, heroic action and devotion to an ideal.

MacDougall,[5] brings out the same principles that are discussed by LeBon. He points out that not every group of human beings gathered together constitutes a crowd in the psychologic sense. There has to be some common focus of interest or sentiment. Some groups cannot be made into a "crowd" because of diversity. Panic is the crudest and simplest example of collective mental life. In a panic there is great intensification of instinctive excitement with its emotion of fear and its impulse to flight. In panic the dominance of the one emotion and its impulse is so complete as to allow no scope for any of the subtler modes of collective operations.

Participation in the mental life of a crowd stirs emotions to a pitch that they seldom or never attain under other conditions. For most people this is intensely pleasurable, or at the other extreme, fatally fascinating. In panic the instinctive fear in man is intensely excited, and he is irresistibly compelled to save himself by flight. This impulse suppresses all others — all habits of self constraint, of courtesy and of consideration of others. The least intelligent minds in the crowd bring the intelligence of the whole down to their level. Emotion replaces reason. The sense of personal responsibility is diminished or abolished. There is a low grade of self-consciousness and no self-regarding sentiment. The mental processes of individuals are profoundly modified by mental interactions with others of the crowd. Conditions become very unfavorable for collective action of a constructive, purposive variety once primitive instinctive drives have begun to express themselves in action.

To quote MacDougall,[5] "We may sum up the psychological character of the unorganized or simple crowd by saying that it is excessively emotional, impulsive, violent, fickle, inconsistent, irresolute and extreme in action, displaying only the coarser emotions and refined sentiments; extremely suggestible, careless in deliberation, hasty in judgment, incapable of any but the simpler and imperfect forms of reasoning; easily swayed and led, lacking in self-consciousness, devoid of self-respect and of a sense of responsibility, and apt to be carried away by the consciousness of its own force, so that it tends to produce all the manifestations we have learnt to expect of any irresponsible and absolute power." It behaves like an unruly child or a savage in a strange situation or a wild beast when restrained.

In times of disaster and after panic, asocial behavior may appear in various other forms. For instance after the Halifax explosion, Prince[6] reported as follows:

> [Before the catastrophe] few people thought that Halifax harbored any would-be ghouls or vultures. The disaster showed how many. Men clamored over the bodies of the dead to get beer in the shattered breweries. Men. . .went into houses and shops, and took whatever their thieving fingers could lay hold of. Then there were the nightly prowlers among the ruins, who rifled the pockets of the dead and dying, and snatched rings from icy fingers. A woman lying unconscious on the street had her fur coat snatched from her back. . . .Then there was the profiteering phase. Landlords raised rents upon people in no position to bear it. Plumbers refused to hold their union rules in abeyance and to work one minute beyond the regular eight hours unless they received their extra rates for overtime. And bricklayers assumed a dog-in-the-manger attitude and refused to allow the plasterers to help in the repair of the chimneys. . . .Many squeezed the uttermost farthing out of the anguish. . .of the homeless men, women, and children. Truckmen charged exorbitant prices for the transferring of goods and baggage. Merchants boosted prices. A small shopkeeper asked a little starving child thirty cents for a loaf of bread.

In the Cocoanut Grove disaster in Boston in 1942 a fire in a night club resulted in the loss of 491 lives and many injuries. There evidently was a major panic, the chief evidence, in addition to eye-witness accounts, being the piling up of 200 victims behind the main exit. Although it is not possible to estimate what the loss of life would have been had there not been a panic, it is reasonable to assume that it would have been less than actually occurred. This disaster did show conclusively that a major tragedy may occur at any time even when least expected, and that a community organized for an emergency is in a far better condition to meet overwhelming demands than one that is not so organized. Every civil-defense worker interested in the medical aspects of disaster would do well to read the symposium describing how one hospital responded to a major peacetime disaster.[7]

Menninger[8] recently reported his observations and those of his colleagues on the victims of the Kansas flood disaster of 1951. In the beginning of the flood period there was a strong feeling of disbelief on the part of the future victims that anything serious could happen to them. Many of them would not move their belongings and later had to be rescued from the second floor of their dwellings. Some of them had to be forcibly evicted by the police. There was much self-incrimination, discouragement, dejection, depression, apathy, con-

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fusion and bewilderment. There was a tendency to be unduly concerned about very minor things, such as the loss of a baby's nightgown, or failure to keep a pet dog with them. They all wanted to talk and share their feelings with others.

Frequently, it was difficult to keep the shelters clean. Cleanliness had to be enforced at times by withholding food until the shelters were presentable. There was no belligerence or agitation.

At the first-aid stations there were many minor physical complaints. Those who lost most and had the least complained less than those who lost very little. The latter were more conspicuous in finding scapegoats, and this tendency was troublesome in the latter stages. There was much blaming of city, county and state officials and of the Red Cross. Many demanded that all their losses be made good by someone.

Nearly all the population responded as if they were threatened personally, whether this was true or not. They all wanted to do something. At first more persons responded to calls for volunteers than could be used, and they got in one another's way. Individuals felt relieved when they got work. Social status disappeared entirely. The workers seemed exhilarated, and pathologic reactions did not occur. The real tragedy was the aftermath, when people returned to their destroyed homes to begin the long and hard work of rehabilitation. At that time calls for volunteers were largely ineffectual.

Reactions to Air Raids in World War II

After considering the characteristics of the group mind, the question arises why panic reactions do not occur more often than they do. Disasters without number occurred during World Wars I and II, and yet there were comparatively few episodes of real panic such as might be inferred from the discussion up to this point. The best study of this subject so far presented has been done by members of the research staff of the Rand Corporation, reported by Janis.[9] The following paragraphs are in effect a review of some of the main findings and conclusions of this group. The observations are mainly based on the experiences of bombed communities in England, Germany and Japan.

There seem to have been no clear-cut differences between the emotional reactions to atomic bombing and to "conventional" bombing. At both Hiroshima and Nagasaki a high degree of surprise was achieved, and the population had no knowledge of the existence of atomic bombs. The conditions were therefore quite different psychologically from those that now prevail in metropolitan areas, where there is considerable tendency to ascribe any unusual explosion to a possible atomic attack. Nevertheless, the people in the two bombed Japanese cities were quickly aware that a disaster of previously unheard of magnitude had struck them. The disaster events that stood out most prominently in subsequent reports of survivors were the flash of the atomic explosion, the blast effects and the presence of large numbers of casualties. From the various reports of the presence or absence of panic no clear-cut picture emerges; the conclusion of Janis[10] seems very sound: "It is probable that overt panic and extreme disorganized behavior occurred in some local circumstances during the two atomic disasters, but it is unlikely that such behavior was widely prevalent among the hundreds of thousands who survived the atomic explosions."

A population caught completely by surprise is at a great disadvantage. The individuals have no idea what to do, even for rudimentary self-protection. In such situations the stage is well set for extreme emotional reactions, whether by single persons or by groups. Fear of the unknown is added to fear of the known, and very few people are able to react intelligently to such overwhelming stimulation. The feeling of utter and complete helplessness does not lend itself to constructive organization for rescue work.

The sight of many maimed and disfigured people is extremely traumatic. Although this may be impossible to avoid, it leads to the suggestion that mobility of the general population should be at a minimum until persons who are delegated to remove the seriously injured have completed their task. Furthermore, some emotional preparation or insulation is desirable for those workers.

Many persons suffer from severe guilt reactions if they pass by injured people asking for help, in the attempt to escape from personal danger or in efforts to reach members of their own families in order to help them. This suggests that each should help people nearest him, which in turn is in keeping with the principle of avoiding useless travel in a disaster area.

There is a considerable tendency for people in a disaster area to find scapegoats on whom the blame for the whole affair can be placed. This tendency is of course not confined to disaster aftermath but is very common in most areas of public and even private life when failure must be explained. Some observers have noted that after the bombing raids in England in 1940 there was widespread resentment against home authorities, as well as against foreigners or refugees, but scarcely any against the Germans. There was some tendency to be more discriminating in placing blame in later stages of the war. It is highly significant from the point of view of the United States that "in a community subjected to air attack any obvious lack of defensive preparation sets off resentment against domestic authorities. Apparent neglect is undoubtedly one of the major determinants of intragroup animosity."[11]

That heavy bombing is very detrimental to civilian morale is quite certain. The more the individual suffered, particularly physically, the more likely

was his morale to decrease. The higher the proportion of "near misses," the lower civilian morale became; the higher the proportion of "remote misses," the higher morale became. Deprivation of community services after raids was detrimental to morale, but not nearly so much so as personal involvement. The same thing could be said about the civilian as Janis[12] said about the combat soldier.

> When a person regards fear reactions as a normal response to a dangerous situation, he is less likely to be disturbed once the danger has subsided by self-reproaches of cowardliness, unmanliness, or other self-accusations which lower self-esteem. Moreover in the face of danger a source of conflict is eliminated if one accepts the notion that he need not fear the loss of status and esteem in the eye of his fellows if he trembles, gasps, and exhibits other marked fear symbols while carrying out his job.

The individual is in a stronger position if he can freely admit his anxiety and deal with it as a reality rather than being forced to misrepresent the situation out of the need to feel like others.

Six types of spontaneous behavior patterns were consistently noted in the civilian population during World War II, particularly among the British[13]:

In the first place, it was noted after each bombing that curious-minded people made extensive tours of the damaged areas. This curiosity was harmful, because it interfered with rescue operations. Some of the people seemed to show a great appetite for strong sensations, and some to derive a positive pleasure in witnessing the scenes of extensive devastation. It appeared as if some individuals were working through their own emotional reactions, so as to be able to go about their affairs normally. Some seemed to be trying to bring their fantasies in line with reality. By actually seeing the destruction wrought, they could think about the tragedy in a more satisfying manner.

Secondly, most of the population reacted quite strongly to all loud noises at the beginning of any series of attacks. They soon became used to this, however, and then reacted only to the most imminent signs of danger; thus a high degree of selectivity was developed, and in this way the least amount of time was lost from useful activity.

Thirdly, many persons became quite talkative during the early stages of danger. This seemed to be a form of emotional release. Those who could admit feeling fear probably were more able to adjust themselves to the trying conditions than those who felt that they must deny it. The increased talkativeness may have been related to the increased sociability that was frequently shown, particularly in the air-raid shelters. It was likewise noted that some comfort was derived from identification with stronger members of the community who were willing listeners, and who displayed a calm, courageous demeanor.

Fourthly, public shelters seemed to be a stronger factor in reducing anxiety than private shelters. The idea that all were in the same boat was apparently a comforting one. Social customs tended to continue to survive as usual in the new and crowded situation. It is quite possible that the lack of a feeling of safety in smaller private shelters was related to the childhood fear of being left alone. It was interesting that many persons derived great satisfaction in seeing important people stay in the danger areas, even under great personal risk to themselves. It was as if the individual thought, "If he can take it I can too."

Fifthly, some persons reacted to bombing by fatalism of one kind or another. "If my name is on the bomb it will get me; otherwise I have nothing to worry about." Many developed increased religious attitudes of one kind or another.

Finally, several people developed systems of various kinds to deny danger or to relieve guilt feelings about any protective measures they may have taken. Some developed an almost compulsive need to go "about business as usual."

There was very little increase in psychoses or other long-continued emotional disabilities except in those who had personalities predisposed to such illnesses. There was a great increase in temporary emotional shock of various kinds manifested mainly in excessive symptoms of anxiety, depression or apathy. There was a slight but definite increase in psychosomatic disorders. Specifically, the percentage of peptic ulcers was greater than usual and there were more symptoms of coronary-artery disease. In addition, cases of exophthalmic goiter and menstrual disorders in women occurred with greater than expected frequency.

Often, the extreme stress produced disorders in children. It seems quite certain that the children tended to reflect quite accurately the attitude of their parents. Bed wetting and extreme nervousness were frequently observed. The incidence of acute emotional disturbances among young children in a community exposed to air raids will tend to vary directly with the incidence of overexcitement and upset among the adults in that community. It is of great interest that many of the symptoms in children were due as much to abrupt separation from their parents as to any dangers they experienced. It appears to be a general consensus that separating children from their mothers to get them out of danger zones was one of the major mistakes of the war.

The reactions of children were somewhat similar to those of adults. After heavy raids there was excessive excitement and apprehension, followed by reactive depressions, apathy, startle reactions, terror states at night, crying spells, or other symptoms of anxiety. Freud and Burlingham[14] noted that all children over two years of age could imagine

fear. These children, then had to contend not only with their own fear but also with the fear that they saw expressed in the faces and attitudes of their elders.

Children have a considerable tendency to use the mechanism of the denial of danger. Some of them seemed to be harmed by witnessing destruction and death as soon as they had become accustomed to control some of their own destructive and aggressive tendencies.

It cannot be overemphasized that evacuation procedures should always include the mother's going with the children if that is possible. Support for this idea comes from Agnes Newton Keith's[15] comments about her seven-year-old son, who had spent four years with her in a Japanese prison camp and had emerged much better off than his parents:

> This was astonishing to me, but reassuring. I could only attribute it to the fact that I did the worrying for him. His one security in camp was me, and as long as I could keep up, he had security. A young child's world is very small, wherever he is. George's six square feet of living space in camp, with me as its walls and roof, was his world, and it was isolated from many terrors that our adult prison camp knew. George's world knew only the things that really happened, only the deaths that were died. Our adult world knew all that might have been, and still might be, besides the pains that were.

Planning for Disaster and Prevention of Panic

A committee of the Group for the Advancement of Psychiatry,[16] under the chairmanship of Dr. Calvin S. Drayer, has recently offered a report entitled "An Introduction to the Psychiatric Aspects of Civil Defense." This report is well reasoned, calm in tone and comprehensive in scope. It points out that the ability of the civil population to withstand stress varies with its emotional or psychologic strength. A strong population needs motivation, a feeling of identification with a specific group and confidence in its leadership. It needs knowledge and understanding of situations demanding solution, and the way this knowledge is transmitted, concerning both its nature and its timing, is very important. The existence of strong social tensions will tend to weaken the population; anything that improves its over-all mental health will decrease the possibility of panic in time of disaster.

This committee considers it worth while to indicate some of the individual and mass reactions that might occur under severe stress. Individually, some few would remain "cool and collected." Most would be stunned and bewildered. These might display automatic behavior and all the concomitant signs of fear and anxiety. The clinical psychiatric syndromes of persistent anxiety states, fatigue states, recurrent traumatic dreams, depressive reactions and rage could be expected.

Mass reactions would probably include panic, apathy, demoralization, scapegoating, rioting and a breaking up of group identification, with regression to sole preoccupation with individual survival.

In the control of disruptive group behavior Dr. Drayer's committee points out the desirability of assuming the possible development of panic and other untoward reactions, together with the making of plans for their control. Prevention itself is the best control, but if panic should start, secondary measures would be urgently needed. Among the specific suggestions are the establishment of road blocks, the furnishing of accurate information at assembly points, the formation of teams to aid in rescue work and the need for training the persons who man the various assembly points. Unauthorized broadcasting should be stopped immediately, and accurate information should be given to all available radio stations as quickly as possible. Sound-casting apparatus in helicopters might be useful in completely disorganized areas. Communication over all channels should be given in a calm, assured voice in simple direct factual terms that can be assimilated as easily as possible by the depressed, fearful, resentful victims of the disaster.

In the treatment of individual psychiatric casualties the experience of combat casualties should be directly applicable — namely, that the earlier treatment is given, the more effective it is likely to be. The early interruption of acute severe anxiety reactions could probably best be accomplished by heavy sedation, a procedure that could be carried out by lay persons with a minimum of medical supervision. "Exhaustion centers" could be operated near other medical installations.

A further statement of the Committee[17] was as follows:

> . . .psychiatrists, as consultants, can contribute to awareness among responsible officials of 1) the potential group and individual emotional problems associated with the various stresses of war, invasion and attack, and 2) the factors which can influence their incidence. It can be expected that out of such awareness will flow a program aimed at the prevention of untoward reaction. Factors of motivation, information, socio-economic organization and general mental health of the population — can be interpreted so that federal governmental agencies and state governments can develop more fully adequate plans.

Caldwell, Ranson and Sachs[18] have presented a thorough review of the factors to be considered in panic and other forms of mass disruptive disorders. They list as the major causes of group panic: tension and insecurity, imitative behavior, suggestibility, rumor, fear of the unknown, lack of preparation and stressful sensory stimuli. Factors that tend to keep group emotions under control include good leadership, group identification and group solidarities, strong motivations and the presence of incentives. Stress is apt to be of much greater seriousness in the absence of community organization and education in principles of mental health. Contributing stresses or supports lie in family life, religious practices, educational systems, industrial practices, social customs and group tensions.

In treatment these authors stress the desirability of reinforcing constructive group and social mechan-

isms. The patient's identification with his community, job or family should be preserved. Secondary gains of illness should be minimized. In fact the therapist should avoid suggestions of illness and disability. Like other observers, they believe that hospitalization should be short, and as near the scene of the disaster as possible, and that the usual hospital atmosphere should be replaced by a series of procedures that suggest quick recovery. Sedation and the treatment of fatigue and exposure go hand in hand with other forms of treatment.

Meerloo,[19] in a recent address before the American Psychiatric Association, stated that some persons are fearful that mere discussion of panic may stimulate fear. It is entirely possible that panic would be more disastrous than bombing itself. He pointed out the necessity for psychiatrists, psychologists, psychiatric social workers and other related persons working together in the prevention of panic. Certainly, the physician would be in a key position in such a program of prevention. Meerloo thought it might be helpful to civil-defense workers generally to understand the clinical approach of psychiatry. This includes a sort of pragmatic approach to unsolved problems: the answers have to be tentative, there is no sureness on the part of anyone, unconscious motives are many, varied and strong, and interpretation should not be made too soon. Tact and restraint are needed in project advisers.

Meerloo further indicated that the individualizing therapeutic approach might be helpful. Behind the masses there are always individual human beings. One should avoid looking at such groups impersonally. Threats and pushing will not work. More needs to be understood about the individual man and his fear, or at least his point of view needs to be considered. How does his mental failure influence his fellows? Every civilian emergency is a new experiment, giving new data and new answers to old problems.

Tyhurst[20] has been a student of disasters for several years, and his recent observations may be helpful. He emphasizes the need for regular rotation of relief personnel. Public announcement and broadcasts should be made with familiar voices if possible. Service uniforms are reassuring early in a disaster, but harmful later. All aspects of community life should be brought to bear on the problem of civilian defense. He indicates that after a civilian disaster there is always a bewildering number of interacting complex situations. There are such diverse questions to consider as group development, public-announcement systems, radio broadcasting, mobilizing taxis and other transportation, food distribution, catastrophic dreams of individuals and attitudes to so-called superior groups in the community. Workers have to be careful not to get bogged down in detail. Hasty generalizations should be avoided. In the early minutes or hours after the crisis leaders must take time to get the feel of the situation and let the various factors shake down.

Tyhurst agrees with the concept that treatment of psychiatric casualties should begin as near the trouble spot as possible. The manner of dealing with them is of great importance in the duration of symptoms. Because of the scarcity of psychiatric personnel, the burden of psychologic management will of necessity rest on those who are not especially trained. The general public should have some idea of what to expect, how to behave toward excited persons and how to make rough evaluation or diagnoses. The average person who survives the disaster wants to see definite evidence that he will be cared for. Since he will have been hurt by loss of friends, by poverty and probably by personal injury, and is dirty and disorganized, some sign of a formative plan will be most welcome, even registration for later receipt of help.

Tyhurst also stresses the importance of good leadership and good organization in public education. Information may sensitize as well as prevent psychologic reactions. It may lead to apathy and disinterest if improperly presented. It should not lead to feelings of helplessness. Leadership is very important to morale. Selection of leaders varies from disaster to disaster. Emergency leaders may replace the nominal leaders, and it is not possible to predict in advance when this will occur. Leaders tend to select themselves; when they do appear it is probably unwise to supplant them. He believes that the details of disaster planning should be worked out on the basis of day-to-day living.

From the considerations offered above and from the literature concerning disaster situations it appears that the most important elements in disaster control are: effective community organization for varying grades of disaster; an educational program designed to let people know what plans have been made, what their role is to be, and that something definite is being done, to strengthen public morale by seeing that energies are directed toward the common enemy rather than in complaints about inefficiency, to obtain equal sacrifice as far as possible, and to get wide diffusion of knowledge of individual and group responses to fear and anxiety; effective leadership that merits confidence so that confusion may be minimized, full and authoritative information may be given before and after a disaster and directions may be issued in time of crisis; avoidance of population movement to prevent the sight of large numbers of casualties to the greatest extent possible; and rapid repair and reconstruction.

General Psychologic Considerations

Organization of the resources of a metropolitan community is exceedingly difficult and complex because of the competing demands of various groups and the inertia of large masses of people. Possibly, the development of numerous organizational plans,

such as that made by the Massachusetts General Hospital,[21] with a flexible over-all co-ordination by state or federal agencies will be workable to the maximum extent. A question that is very difficult to answer is that of the effect of stirring up anxiety to get a program carried out. From a random sampling of individual opinion of persons who have listened to talks attempting to create urgent interest in civil defense, I have gained the impression that in many instances so much anxiety was created that individuals could not cope with it. In effect they have used the mechanism of simple denial: "If it is going to be like that I will have nothing to do with it until it really comes." The lectures or discussions that end on a hopeful, constructive note, however, help to relieve anxiety by channeling it into purposive constructive action.

Nevertheless, it is necessary that preparations for disaster be carried out. Possibly, much anxiety will have to be generated; in fact it is unavoidable. It can be brought out, however, in gradual ways. MacCurdy's[22] observations have indicated that persons exposed to air raids, but rather remotely so, tend to have their morale raised; whereas those who are exposed in a more intimate fashion lose morale. This is in keeping with Adrian's[23] comment, made at the Harvard Tercentenary, that "our behavior will be most effective when there is enough emotional tension to arouse the activity of the forebrain but not enough to submerge it in a stereotyped response."

The necessary questions that must come up if a community is to be prepared adequately for disaster may be brought out in discussion groups. This presupposes that the discussion leaders are well fortified with information about the responses of groups of people to great hazards. Discussion groups might have the additional advantage of serving as a means of conveying the attitudes of large numbers of people to those who are responsible for disaster planning.

It has been pointed out above that one of the most traumatic experiences that a person could have was the realization that he had refrained from giving help to someone either while seeking his own safety or looking for other members of his family. This difficulty might be avoided if the sentiment could be built up that everyone should help those who are in the immediate vicinity. If all persons in a disaster area could take this attitude, any one person could help persons nearby with the reasonable hope that any injured member of his own family might be taken care of by whoever happened to be near. If properly handled this "other-person-centered" attitude might be quite helpful in stimulating morale. Certainly, it is related to the idea that those who are in training are really organized to help neighboring towns. If any town or city is overwhelmed by a major disaster, it is to their neighbors that they must look for help rather than to their own efforts. In effect this means that one can help himself only by helping others, and it calls for an altruistic and idealistic attitude on the part of everyone.

This problem must be approached with an awareness of the tremendous complexity that it shows. There are many questions that simply cannot be answered. What is good for one town may not be good for another. What will work in one neighborhood will be impossible in another. Instead of searching for rules and regulations one must search for general principles of human behavior under stress. One must learn how to think about people in trouble. Group discussions are held to bring about these attitudes because members of a group will disagree among themselves. Working out the areas of agreement and disagreement helps to build insight into the larger areas of this type.

In community planning for the management of fear during disasters it is advisable to emphasize that one is looking toward any accident that may occur in the communities, of which an atomic explosion may be only one, even though it is the most dreaded. In an alert community organization there is no room for fatalism. Whatever is done cannot make an atomic attack less probable — that is a diplomatic and military problem. Any good preventive measure should, however, reduce the extent of the damage from the disaster while improving the community's resources to handle it if it does come.

Any educational measures taken should be broadly based. Extensive, intricate plans will be of little use if the people in the community do not know what is to be expected of them. Janis[24] lists as vitally important two main ways by which emotional control can be fostered: preparatory education and on the spot communication. In both of these the information for all the people must be simple, direct, consistent and often repeated. The bulletin on atomic disaster issued by the Civil Defense Agency of Massachusetts is an example of such communication and has apparently not generated excessive anxiety. It is also entirely possible that marshaling the community's resources on behalf of civil defense might have secondary values in improving motivation and reducing vulnerability to breakdown from other types of stress. The positive "rewards" that come to a community when its citizens join together in a common cause for an object that is not entirely selfish are valuable.

Summary

Mental health is an all inclusive field. Civil defense may seem beyond the capability of modern metropolitan industrial cities. Consideration of the two of them at once seems like compounding confusion. Yet a review of this sort discloses a surprising amount of agreement of opinion. There is a general consensus that the reactions of the

individual are paramount. What he knows, thinks, feels and does determines to a large extent what the group will do. Well thought-out disaster plans of a flexible nature are imperative. The importance of vital leadership is stressed by all observers. The larger the proportion of calm people in a crowd, the greater the possibility that the group will remain calm. The higher the general level of mental health of the community, the more likely it will be to adapt itself to conditions of severe stress. Educational measures can and should be realistic: they must be simple, clear, thorough and widely based. Communication after a disaster should be clear, concise, calm in tone and often repeated. There are no sure answers — what matters is that great numbers of people know the questions and the difficulties involved.

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MEDICAL INTELLIGENCE

GALLSTONE ILEUS, VOLVULUS OF THE SMALL INTESTINE, INCARCERATED FEMORAL HERNIA AND PERITONITIS*

Report of a Case

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BOSTON

THE combination of gallstone ileus, volvulus of the small intestine, incarcerated femoral hernia and diffuse peritonitis is sufficiently unusual to warrant a report. The probable sequence of events in the development of the clinical picture makes this case of added interest.

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Case Report

L. H. (BIH M20709), a 74-year-old woman, entered the hospital because of pain in the lower abdomen, nausea, vomiting and obstipation of 2 days' duration. She had been quite well until 2 years prior to entry, when she had a 3-day episode of severe pain in the right upper quadrant, tenderness, nausea and vomiting. At that time she was told that she had "gall-bladder trouble." She recovered completely from this attack and remained entirely well until 2 days before admission, when nausea, colicky pain in the lower abdomen, obstipation and vomiting suddenly developed. These symptoms increased in severity up to the time of admission.

Physical examination revealed an obese, apathetic, uncooperative but well oriented woman. The tongue was dry, red and smooth at the edges. The scleras were clear. The chest was emphysematous. The heart sounds were distant. The abdomen was markedly distended and exquisitely tender to palpation throughout. Peristalsis was diminished. There was a firm, irreducible, nontender mass, 6 cm. in diameter, in the right femoral region. Rectal and vaginal examinations were negative.

The temperature was 101.4°F., and the pulse was weak, thready and rapid. The respirations were labored. The blood pressure was 140/70.

Laboratory studies revealed a white-cell count of 13,600 and a hemoglobin of 16 gm. The urine had a specific gravity of 1.026 and was otherwise normal.

A "scout" film of the abdomen showed several dilated arched loops of small intestine with fluid levels.

The preoperative diagnosis was strangulated right femoral hernia with peritonitis. A Miller-Abbott tube was passed to the pylorus, and 1500 cc. of 5 per cent dextrose in physiologic (0.85 per cent) saline solution, with 500 mg. of aureomycin, was administered intravenously. Three hours after admission, under nitrous oxide, oxygen and ether anesthesia, the femoral hernia was exposed through an inguinal incision. The sac was found to contain a mass of incarcerated adherent omentum. Purulent exudate poured from the peritoneal cavity. The inguinal incision was rapidly extended upward so as to give free access to the intraperitoneal disease, the nature of which now became clear. A cord-like segment of omentum extended across the peritoneal cavity like a taut bowstring from its origin to the femoral sac. A loop of gan-

grenous ileum, held firmly beneath this cord, had rotated 180° clockwise on its axis, completely cutting off its blood supply. The intestine both proximal and distal to the necrotic loop was distended. The exploration was therefore continued distally until collapsed small intestine was found near the ileocecal region. At this point a 2-cm. gallstone was found impacted in the bowel. The peritoneal cavity contained about 1000 cc. of foul-smelling, cloudy fluid, which showed leukocytes and gram-negative bacilli on smear, but did not yield growth on culture. Further exploration was not carried out because of the precarious condition of the patient.

The gallstone was removed through an enterotomy, and the gangrenous intestine resected and continuity restored by end-to-end anastomosis. The incision was closed in layers, with drainage of the subcutaneous tissues; 500 cc. of blood was administered during the operation. The patient left the operating room in poor condition.

The postoperative course was stormy for the first nine days. There was a remittent fever (temperature of 99 to 101.5°F.) and a leukocytosis (white-cell count of 13,000 to 20,000). Distention was reduced by a Miller-Abbott tube. Peritonitis was controlled by aureomycin administered intravenously in doses of 500 mg. every 12 hours for the first 9 days, followed by 500 mg. every 6 hours orally for 5 days thereafter. Jaundice, probably due to the intravenous aureomycin therapy,[1] developed on the 2d day and gradually subsided during the 5 days following discontinuance of aureomycin therapy. Superficial wound sepsis due to *Aerobacter aerogenes*, *Proteus vulgaris* and *Pseudomonas aeruginosa* developed. In-vitro sensitivity studies revealed *A. aerogenes* and *P. vulgaris* to be very sensitive to chloramphenicol (Chloromycetin) and resistant to streptomycin, aureomycin and terramycin. *Ps. aeruginosa* was resistant to all 4 antibiotics. Consequently, aureomycin was omitted, and chloromycetin was given, with prompt control of the wound infection. A severe stomatitis, probably due to antibiotic therapy, developed. This failed to respond to intensive parenteral vitamin therapy, but subsided slowly after discontinuance of all antibacterial agents. The patient was finally discharged well on the 32d postoperative day.

Discussion

The probable sequence of events leading to the clinical picture could now be reconstructed. The small intestinal obstruction was probably initiated by impaction of the gallstone in the terminal ileum. With the associated violent peristaltic activity, a loop of proximal ileum prolapsed under the cordlike omentum and subsequently strangulated because of progressive distention and rotation of the loop.

The difficulty in making a preoperative diagnosis of gallstone ileus and its high mortality are well known.[2-5]

The importance of thorough exploration through adequate incisions is well demonstrated in this case and needs no further comment.

Summary

A case of incarcerated femoral hernia, volvulus of the small intestine, gallstone ileus and diffuse peritonitis with recovery is reported.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

Weekly Clinicopathological Exercises

FOUNDED BY RICHARD C. CABOT

BENJAMIN CASTLEMAN, M.D., *Editor*

VIRGINIA W. TOWNE, *Assistant Editor*

CASE 38321

Presentation of Case

A fifty-four-year-old man was admitted to the hospital because of intermittent abdominal pain.

Six months before admission, shortly after returning from a trip to Mexico, the patient had fever (maximum temperature of 101°F.), malaise and generalized aches for two weeks and diarrhea for one day. Urinalysis was negative. The white-cell count was 5800, with a few abnormal lymphocytes and monocytes in the blood smear. A number of blood smears were negative for malarial parasites, agglutination tests for brucellosis, typhus and typhoid fever were nondiagnostic and a heterophil-antibody test was negative. He recovered spontaneously.

Two weeks prior to entry he had the onset of mild general fatigue, associated with a low-grade fever (maximum temperature of 100°F.), low backache and generalized abdominal aching; the abdominal discomfort was steady and tended to localize in the right lower quadrant. Physical examination showed a soft abdomen, slight lower abdominal tenderness, a feeling of fullness and resistance in the right lower quadrant and normal peristalsis; rectal examination was negative. The white-cell count was 11,000, with 59 per cent neutrophils, 6 per cent stab cells, 23 per cent lymphocytes and 12 per cent monocytes. During this episode he was constipated, but passed gas by rectum and had a feeling of abdominal fullness as if he needed to move his bowels; he was anorexic but had no nausea or vomiting. After forty-eight hours he improved somewhat but continued to have the same general symptoms for a few more days; after the first forty-eight hours his bowels moved, but with less frequency than usual. For the week prior to entry he was well with no complaints, until two days before admission, when a low backache followed by low abdominal distress developed. These symptoms remained constant dur-

ing the day prior to admission, and examination showed a soft, nontender abdomen, normal peristalsis, temperature of 99°F. and a white-cell count of 13,500. He had a normal bowel movement the morning before admission.

The patient's appetite had been poor, but there had been no weight loss. He did not feel well generally, but had not had nausea, vomiting, diarrhea, melena, urinary symptoms, dyspnea or decreased exercise tolerance. He had had a vague right-lower-quadrant ache with awareness of the cecal area for many years. At the age of ten he had had "jaundice," at the age of nine an appendectomy, and at the age of seven surgical removal of cervical lymph nodes, allegedly tuberculous. He was a mining engineer and had traveled extensively.

Physical examination revealed a surgical scar in the right side of the neck. The lungs and heart were normal. There was a right-lower-quadrant surgical scar and just medial to this there was a consistently well localized tenderness, with a suggestion of fullness in this area. There was no definite spasm and no palpable organs. Peristalsis was present but varied somewhat, most being quiet but occasional ones being high pitched and occasionally coming in rushes. Rectal examination was negative.

The temperature was 99.8°F., the pulse 70, and the respirations 18. The blood pressure was 120 systolic, 80 diastolic.

The urine had a specific gravity of 1.020 and was normal. Examination of the blood showed a hemoglobin of 14.6 gm. and a white-cell count of 10,800, with 77 per cent neutrophils, 20 per cent lymphocytes and 3 per cent monocytes. The sedimentation rate was 2 mm. in 15 minutes, 12 mm. in 30 minutes and 31 mm. in 60 minutes. A stool gave a negative guaiac reaction, did not contain any amebic ova or cysts and was negative for pathogens on culture. A roentgenogram of the chest was normal. An abdominal film showed no definitely dilated loops of small or large bowel. The left-kidney outline appeared normal; the right was not well visualized. The psoas-muscle shadows were clear. Barium-enema examination showed no evidence of gross obstruction; there was a considerable amount of fecal material present so that the examination was adequate only to exclude a large obstructing lesion. A gastrointestinal series showed a normal esophagus, stomach and duodenum. The barium filled the entire small bowel and the colon to the hepatic flexure. The small bowel appeared to be largely in the left half of the abdomen except for the loops of ileum that were in the pelvis. There was some tenderness in the right side of the abdomen in the area where there were relatively few loops of small bowel, but no mass was palpable. At the end of six hours barium was in the ileum and colon.

For the first three days the patient had a temperature of 100°F., but subsequent to this he was afebrile. Enemas produced some relief of the abdominal discomfort, which was usually short lasting, but did not affect the right-lower-quadrant tenderness. His appetite was good. He had sporadic attacks of more severe abdominal pain accompanied by some abdominal distention and usually followed by the passage of stool, sometimes liquid, and large amounts of gas, with some relief of symptoms. On the tenth day an operation was performed.

Differential Diagnosis

Dr. Chester M. Jones*: There is only one important point in this case: there should have been, and was, a decision to operate because of the inability to make a diagnosis. Having said that, I am obligated to try to make a diagnosis.

The symptoms were those of partial obstruction of the bowel probably at the level of the ileocecal valve, either in the ascending colon or in the terminal ileum. Obviously the obstruction was nowhere near complete, and never had been. There was a history, antedating the trip to Mexico by many years, of right-lower-quadrant discomfort and distress, not very marked, but probably in the same category as the more marked symptoms that brought the patient to the hospital. I think the situation was a chronic one that was capable of becoming worse and also of improving at least temporarily.

The possible causes of right-lower-quadrant pain, some interference with bowel habits and localized right-lower-quadrant tenderness are fairly numerous. They can be listed under several headings. One heading is that of a mechanical defect with or without congenital malformation such as a volvulus of the cecum, a diverticulum of the cecum or an intussusception. Volvulus of the cecum may cause acute attacks and interfere with blood supply; then, too, there should be blood in the stools. Diverticulum of the cecum at times is associated with obstructive episodes, but it must be a very rare condition; it should be associated with actual infection and perforation of a diverticulum and a more acute episode than this man presented. An intussusception implies the possibility of an intrinsic tumor that moves to a narrower portion of the gut, temporarily occluding it, but then reduces itself, leaving the patient free of symptoms. Intussusception from a tumor is unlikely because despite the degree of pain that was present on several occasions, there was no blood in the stool. The intussusception could have been due to neoplasm in the gut — lipoma, fibroma, sarcoma or adenocarcinoma of the ileum, or adenocarcinoma of the cecum, all of which may partially obstruct. Another possibility is lymphoma of the mesenteric lymph nodes. It is difficult for me to believe that the more malignant types of lesions could account for this situation, especially if it had been going on intermittently for some time. By this time the patient would have lost weight and would have had anemia; certainly if he had cancer of the cecum

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arising near the ileocecal valve, he would have had a pronounced anemia by this time.

Another heading could be that of a gradually infiltrative inflammatory process of a granulomatous nature in the region of the ileocecal valve — that is where I am assuming the condition lay — such as tuberculosis, regional ileitis or an infection associated with the stump of an appendix, which had been left in at the original appendectomy done in 1907. Recurrent attacks of right-lower-quadrant pain with fever can occur from this cause. One could consider parasitic disease, assuming that the trip to Mexico was not a "red herring." The patient actually developed gastrointestinal symptoms with a certain amount of diarrhea although it was very short lived; he was a mining engineer who traveled extensively and may have been exposed to an amebic infestation before the onset of symptoms and may have had an amebic granuloma in the region of the cecum.

Some of these conditions can reasonably be ruled out. In the first place, this man had had his appendix removed; therefore, residual appendiceal disease seems quite unlikely; I mentioned it only because once in a while it is encountered. Tuberculosis in this area is possible, — a stenosing type secondary to ulceration, — but it would certainly be unusual to find tuberculosis in this area without any evidence of tuberculosis elsewhere. Nevertheless, primary tuberculosis of this area can occur. Although regional enteritis involving only the terminal ileum could underlie this condition, the history does not suggest it. All I can say is, if it was regional enteritis, it falls into the unusual group in which the disease is never suspected until the diagnosis is made at operation.

Although I suspect the barium-enema examination was not too satisfactory, it may give me a clue. May I see the x-ray films?

Dr. James J. McCort: The examination of the chest was negative. A plain film of the abdomen shows no dilated loops of small or large bowel. In the gastrointestinal series the stomach and duodenum are normal. When the barium passes into the small bowel, it is seen that the small-bowel loops are displaced to the left side. The visualized segments of the small bowel show no localized areas of dilatation or constriction.

Dr. Jones: This normal-looking terminal ileum indicates that there was no reason to suspect tuberculosis or regional ileitis involving the terminal ileum.

Dr. McCort: On the barium-enema examination it can be seen that the colon contains a large amount of feces. No gross lesion is seen between the rectum and cecum. A slight degree of mucosal swelling may be present.

Dr. Jones: There is no evidence of a diverticulum in this area or in any other area so I think I can rule that out.

That leaves me with a patient with recurrent attacks of right-lower-quadrant pain with leukocytosis and with variable tenderness. On one occasion there was no tenderness; then on the same day somebody found a tender spot in the same area that was tender during the x-ray examination. This film suggests the possibility that there is something displacing the loops of small bowel; that is a variable sign in which one cannot place absolute confidence. Would you agree with that, Dr. McCort?

Dr. McCort: Yes; it varies with the amount of small-bowel filling.

Dr. Jones: Nevertheless, it fits in with the clinical findings of a sense of fullness or mass in this particular area and local tenderness. Very rapidly, I tend to rule out volvulus or intussusception from a tumor or a diverticulum. I think the evidence for an intraluminal new growth is lacking. If there was a long pedunculated polyp that could drop down in the region of the ileocecal valve it had not been demonstrated. I suspect very strongly that this was not present because the episodes lasted too long for intussusception from a polyp without much more evidence of serious interference with the blood supply of the tumor, and therefore bleeding as well. I think this clinical picture was on an inflammatory basis. I cannot conceive just what was going on outside the ileum, without any more information than I have at the present time. There is one more bit of evidence against old tuberculosis: there was no evidence of calcification in the region of the root of the mesentery.

That leaves me with a complete inability to make a reasonable diagnosis. The two diagnoses I favor — neither one is very logical — are a localized area of tuberculosis or infection in an appendiceal stump. There was nothing unusual about the appearance of the cecum implying nonrotation or unusual mobility that would make the possibility of volvulus a reasonable one in this particular case. I am sure that the patient should have been operated upon. I would be interested to know what the preoperative diagnosis was, but I would be surprised if a flat diagnosis was made preoperatively.

Dr. Walter Bauer: Why did you not go back to the possibility of a congenital anomaly as the cause of the pain over such a long time?

Dr. Jones: That is a reasonable question, but there was no evidence of it. The congenital anomalies in the region of the cecum that can become involved in a volvulus are localized diverticula or Meckel's diverticulum. Meckel's diverticulum could do this, but again with repeated episodes I would expect some bleeding. An appendix epiploica that became caught in this area, I suppose, is a possibility, but I have no means of even guessing on that.

Dr. Bauer: Do large mesenteric cysts ever occur in this part of the belly?

Dr. Benjamin Castleman: You may find them almost anywhere, although they are usually higher up.

Why are the small-bowel loops pushed over in the x-ray film?

DR. JONES: In this lower area the small bowel appears to be moved to the left. That is not unusual; we frequently see x-ray findings like that; when the patient is put into a different position, the bowel may go back into place. When the bowel loops are consistently displaced, I think one has to suspect extraluminal disease. I am wondering whether it might have been due to enteritis with fistula formation and abscess surrounded by loops of small bowel, but no mass was felt at any time. I should like to put tuberculosis first because it seems to fit the picture as well as anything; I do not think it is a very good diagnosis.

A PHYSICIAN: I would like to ask Dr. Jones if he also considered tuberculous peritonitis?

DR. JONES: I see no reason for making a diagnosis of tuberculous peritonitis on the basis of the physical findings.

CLINICAL DIAGNOSIS

Tuberculous mesenteric lymphadenitis.

DR. JONES'S DIAGNOSIS

?Tuberculosis of mesenteric lymph nodes.
?Infection in appendiceal stump.

ANATOMICAL DIAGNOSIS

Malignant lymphoma, stem-cell type, of mesenteric lymph nodes.

PATHOLOGICAL DISCUSSION

DR. CASTLEMAN: Dr. Richard Stetson saw this patient and I believe went through the same pros and cons; finally the patient was operated on as Dr. Jones suggested. Dr. Arthur W. Allen found a mass of lymph nodes in the distribution of the superior mesenteric vessel and closely adherent to it. Since he could not remove the mass without sacrificing this vessel, he took out only one lymph node, which I cut in the operating room. The lymph node looked almost caseous and had a little fleck of calcium in it so when I left the operating room I thought it would prove to be tuberculosis, and saved some for guinea-pig inoculation. Microscopically, it turned out to be a malignant lymphoma of a very highly undifferentiated form; we subsequently called it a stem-cell lymphoma, according to the Gall and Mallory* classification. The patient received x-ray treatment and left the hospital twenty-seven days postoperatively.

*Gall, E. A., and Mallory, T. B. Malignant lymphoma: clinicopathologic survey of 618 cases. *Am. J. Path.* 18:381-429, 1942.

CASE 38322

PRESENTATION OF CASE

First admission. A forty-three-year-old Chinese laundryman entered the hospital because of repeated bouts of hemoptysis.

The patient had always had a morning cough productive of small amounts of gray mucoid material, but coughing of about a cupful of blood had begun eighteen months before admission and occurred not more frequently than once a month.

Physical examination showed the chest to be clear anteriorly but to be somewhat dull at the bases. Urinalysis and stool examination were negative. Blood-tinged sputum was present, but the sputum was negative for acid-fast bacilli. Roentgenograms of the chest showed findings consistent with bilateral lower-lobe bronchiectasis, and a bronchogram confirmed this. Two weeks after admission the left lower lobe was removed. Pathological examination showed bronchiectasis, tuberculosis and chronic pneumonitis.

Final admission (five years later). Since the last admission the patient had been free from cough, hemoptysis and expectoration. One month before entry abdominal pain and fullness developed. There was also a feeling of anorexia and occasional bouts of vomiting of small amounts of blood. The urine had been dark but occasionally was red. For some time an occasional stool had been black. Scleral icterus was observed by friends prior to entry. Two days before admission bilateral ankle edema was noted.

The patient, who had been born in Canton, had been in the United States for more than thirty years. There was no history of habitual use of alcohol or exposure to toxic agents.

Physical examination showed a seriously ill man with a definitely icteric skin and scleras. The neck veins were flat. There was a well healed left-thoracotomy scar. Diminished breath sounds at both bases were noted, and the percussion note was dull in the same area. The point of maximal impulse of the heart was 11 cm. from the midsternal line in the fifth intercostal space. Grade II, apical, systolic and Grade III, pulmonic, systolic murmurs were heard. The pulmonic second sound was greater than the aortic. Fluid bulged both flanks, and there was demonstrable shifting dullness. The liver edge was percussed 5 cm. below the costal edge. The spleen was not palpable, nor were any abdominal masses felt. A ++ pitting edema was present from the dorsum of the foot to the knee. Examination of the central nervous system was negative.

The temperature was 98°F., the pulse 90, and the respirations 20. The blood pressure was 120 systolic, 70 diastolic.

The urine was red, had a specific gravity of 1.025 and gave a negative test for albumin and glucose and a ++ test for bile; the sediment contained 5 white cells per high-power field but no red cells. Examination of the blood showed a hemoglobin of 10 gm. and a white-cell count of 3500, with a normal differential. The total protein was 6.66 gm., the albumin 2.92 gm., the globulin 3.74 gm., the nonprotein nitrogen 22 mg., the bilirubin 4.4 mg. direct, 6.4 mg. total, the sugar 70 mg., the cholesterol 196 mg. and the cholesterol esters 77 mg. per 100 cc.; the prothrombin time was 33 seconds (normal, 17 seconds), and the cephalin flocculation +++ in

twenty-four and ++++ in forty-eight hours. Multiple stool examinations were guaiac negative. Ninety cubic centimeters of turbid fluid removed by abdominal paracentesis as a diagnostic procedure was negative for tumor cells on cytologic examination. A chest film showed atelectasis resulting from a high diaphragm, strands of increased density in the remaining lung in the left side of the chest and a honeycomb pattern at the right base. The heart appeared to be transverse rather than enlarged. A gastrointestinal series demonstrated esophageal varices. Examination of the stomach was handicapped by the abdominal distention and tenderness; the pattern of the mucosal folds suggested gastric varices but no areas of ulceration or rigidity. There was evidence of extrinsic pressure along the greater curvature, apparently caused by a large spleen.

A rapidly progressive downhill course with a decided increase in abdominal girth and tension was accompanied by anorexia. Jaundice became intense. Mercuhydrin produced little or no diuresis. The low oral intake was supplemented with 25 per cent dextrose and water intravenously and intravenous administration of fats to make a daily intake of 2200 to 2500 calories. Twenty-four hundred cubic centimeters of turbid, yellow fluid was removed by abdominal paracentesis. After this the liver could be palpated 3 to 4 fingerbreadths and the spleen 1 to 2 fingerbreadths below the costal margin. Both organs were tender, but no definite abnormalities of their surfaces could be made out. Urinary excretion diminished, with complete anuria on the thirteenth day, which was the day of death.

Differential Diagnosis

Dr. Joseph W. Gardella*: To begin with, it seems almost certain that this patient had diffuse hepatic fibrosis. The insidious onset of vague abdominal symptoms and ascites, the edema confined to the lower legs, the gastrointestinal bleeding, the jaundice and the hepatosplenomegaly in association with anemia, leukopenia, impaired liver function and varices constitute overwhelming evidence for the presence of long-standing diffuse hepatic fibrosis. The most reliable finding in support of this conclusion is the x-ray evidence of portal hypertension in the presence of liver disease. According to Himsworth,[1] this combination is invariably the result of long-standing fibrosis of the liver. If liver disease does not accompany portal hypertension, portal-vein thrombosis must be considered, since the pattern of collateral circulation may be identical in these two conditions. The obvious liver disease in this case points to hepatic fibrosis rather than portal-vein thrombosis as the primary cause of the portal hypertension. I wish to make this distinction especially clear since I think that portal-vein thrombosis may have developed late in the course of the primary disease, which appears to have been portal cirrhosis.

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Yet there are several unusual findings that must be reconciled with this diagnosis. Let me consider first the red urine. In the presence of liver disease the mention of red urine immediately suggests porphyrinuria. Cirrhosis is frequently accompanied by a marked increase in the excretion of urinary porphyrins. If the urine is alkaline they may escape detection since the colorless chromogen, prophobilinogen, is changed to the red pigment, prophobilin, only at an acid pH. Knowledge of the urine reaction would be helpful in this respect.

Dr. David Kahn: The pH of the urine was 5.5 on admission.

Dr. Gardella: I really do not know what else to consider. The absence of hematuria or evidence to incriminate appropriate medications or dyes indirectly supports the assumption that the red color was due to porphyrins. This explanation is at least consistent with a diagnosis of cirrhosis.

Since I am discussing the urine it is perhaps permissible to skip to a consideration of the terminal renal shutdown. There was really little to suggest primary kidney disease so I judge that the oliguria was of extrarenal origin, possibly hepatic. Now the relation between hepatic and renal failure is much disputed although it is generally agreed that they do occur simultaneously with impressive frequency. Furthermore, several physiologic explanations for this relation exist and may be applicable to this case. Ralli[2] has demonstrated the presence of an antidiuretic substance in the urine of patients with cirrhosis of the liver. Secondly, sodium and water retention is characteristic of cirrhosis, and potassium deficiency as a consequence may further impair urine flow. Under these circumstances mercurial salts often fail to increase excretion of sodium. The mention of increased abdominal tension brings to mind the experiments of Thorington[3] which demonstrated that abdominal compression reduces renal plasma flow, glomerular filtration rate and urine flow. Then, again, the report of increased abdominal pressure suggests that thrombosis of the inferior vena cava may have been responsible for the urine failure in this case. Whatever the mechanism of the terminal renal failure, it is easily reconciled with cirrhosis.

The turbid ascitic fluid, however, is not so easily dismissed, for in cirrhosis it is usually clear. Apparently, the fluid contained no tumor cells. Although unreported, a cellular infiltrate of some type was probably present since something made the fluid turbid.

Dr. Kahn: There is no mention in the record that the fluid was examined except for tumor cells.

Dr. Gardella: Perhaps the fluid was milky, as occasionally happens in cirrhosis. However, I prefer to postulate cellular infiltration, especially in view of the abdominal tenderness, which seems rather extensive for uncomplicated cirrhosis — extensive enough, in fact, to handicap the radiologist, and that is impressive. I am forcing the possibility of peri-

tonitis. The absence of fever and the low white-cell count mitigate against bacterial, but not necessarily against tuberculous, peritonitis. After all, tuberculous peritonitis frequently complicates cirrhosis especially in Asiatics; this patient was an Asiatic with cirrhosis and proved pulmonary tuberculosis. However, the turbid fluid itself is unusual.

But the big gun threatening my defense of cirrhosis is the unusually rapid course of the disease. Although I need not surrender entirely, I think I certainly must compromise with an additional pathologic process to account for the rapid deterioration. Upon just what process to compromise is the chief obstacle. Acute hepatitis, liver necrosis, portal-vein or hepatic-vein thrombosis and hepatoma are reasonable considerations. I get the impression that the rapid and extreme degree of ascites formation in the presence of nearly 3 gm. per 100 cc. of serum albumin was due to a terminal obstructive process in the portal or hepatic veins. Neither an inflammatory nor a necrotizing process in the liver is likely to do this. Furthermore, if either hepatitis or acute necrosis initiated the onset of symptoms, I think the terminal phase would have been considerably less than forty-three days, especially with necrosis.

What I really need is something to account for the large tender liver, the increasing failure to excrete bile, the accelerated formation of ascites and the rapid deterioration. Considering the patient's race and the evidence for cirrhosis, carcinoma of the liver seems a suitable choice. Then one need only postulate a terminal invasion of the portal vein to bring the findings together — all the findings but the turbid ascites, which is still out of line. Tuberculosis may account for this if it existed.

I am invited to discuss schistosomiasis, which I refuse to do. Banti's disease I consider a variant of cirrhosis. Weil's disease I merely mention. The evidence that heart disease was complicating this picture is unimpressive. The pulmonic systolic murmur may have been the result of displacement of the great vessels.

Clinical Diagnosis

Laënnec's cirrhosis.
?Acute yellow atrophy of liver or carcinoma of liver.

Dr. Gardella's Diagnoses

Portal cirrhosis, with hepatoma.
Portal-vein or hepatic-vein thrombosis.
?Tuberculous peritonitis.
Pulmonary tuberculosis.
Bronchiectasis.

Anatomical Diagnoses

Portal cirrhosis, post-necrotic type.
Hepatoma, with invasion of smaller radicles of portal and hepatic veins and metastases to lungs.
Congestive splenomegaly.
Esophageal varices.
Ascites.
Pulmonary tuberculosis, apexes, quiescent.
Bronchiectasis, right lower lobe.

Pathological Discussion

Dr. Kahn: The opinion of the clinicians caring for this man while he was in the hospital agreed entirely with that just outlined by Dr. Gardella. It was unanimously agreed that the disturbed liver function with the portal hypertension was indicative of portal cirrhosis, but that the course was much too rapid to be explained by this alone. As possible additive lesions to explain this rapid course hepatoma, acute necrosis, tuberculous peritonitis and hepatic-vein or portal-vein thrombosis were suggested by different observers.

At autopsy the peritoneal cavity contained 2500 cc. of blood-tinged serous fluid; there was no evidence of peritonitis. Possibly, the turbidity described was due to red blood cells. The liver, which weighed 1400 gm., was coarsely nodular, with bands of fibrous tissue dividing nodules of various sizes. Superimposed on this pattern was a 10-by-10-by-8-cm. conglomerate of softer, yellowish-gray nodules situated in the anterosuperior part of the right lobe, and a sprinkling of nodules of similar tissue, varying from 1 to 3 cm. in diameter, throughout the whole liver. The main portal and hepatic veins were patent and unremarkable.

Microscopically, there was an advanced portal cirrhosis of the post-necrotic type, and superimposed on this a primary liver-cell carcinoma or hepatoma, which was much more widespread and extensive than the impression gained from gross inspection. Scattered throughout every section, infiltrating the fibrous tissue and invading almost every vein, were clumps and strands of tumor cells; these tended to mimic the liver cells in shape and pattern but were somewhat larger; many contained mitotic figures.

There were numerous small metastatic nodules scattered throughout the lungs; it was interesting that in both the liver and the lung some of the tumor cells contained a fine sprinkling of yellowish-brown pigment indicating that they were capable of some degree of function. In addition in the lungs, there was bronchiectasis in the right lower lobe, and in the apical scars a number of foci of quiescent fibrocaseous tuberculosis.

The spleen weighed 530 gm. and histologically showed marked congestion and fibrosis, with a number of siderotic nodules. The esophagus contained a number of large varices. The heart was normal, so that the murmurs heard must have resulted from either a functional or a mechanical cause that we were not able to demonstrate. We are also unable to offer any morphologic explanation for the renal shutdown, since the kidneys were normal.

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FREEDOM FROM FEAR

Among the many problems of civilian defense, few are more basic than the reaction of populations to the destruction from wholesale bombing of which the experience in Great Britain, Germany, and Japan was but a sample. The Medical Progress report in this issue of the *Journal* calls attention to this often neglected aspect of preparedness and suggests means of ensuring that the civilian population will not be thrown into helplessness and panic at a time when the co-operation of every man, woman and child is vital. From this point of view a significant part of civilian defense becomes a campaign of protection against hysteria through fear of the dreadful results of bombing rather than a question of warding off the attack itself. If the facts are understood and their implications accepted, a great step forward will have been taken; if, because of dread of the horrors to come, Americans refuse to face the disquieting possibilities, they are inviting disaster even more serious than the devastation itself — a state of chaos that could paralyze efforts to recover and to retaliate. As the report points out, "Fear of the unknown is added to fear of the known, and very few people are able to react intelligently to such overwhelming stimulation."

The immediacy of the problem is underscored by the recent call for thousands upon thousands of volunteer aircraft spotters and the warning by military authorities that, in present circumstances, an enemy could break through air defenses in sufficient numbers to destroy any one — or a number — of large cities at one blow. Strategic bombing, of the kind accomplished with such devastating effect on German industrial centers, is aimed at complete paralysis and confusion in vital areas of production by means of catching the population off guard. Future Pearl Harbors may not be prevented, but what the report calls "emotional control" may go far toward averting the panic that, to the enemy, is a tremendous advantage of a surprise attack. Preparatory educational programs, widely disseminated and simply and clearly presented, will do much to deny any aggressor the greatest profit resulting from unprovoked and unannounced atomic bombing. There is no room, in this philosophy of preparation, for the belief that the most powerful potential enemy is incapable of devastating air attacks or likely to be restrained by humane considerations from attaining the tactical superiority gained by a surprise attack on civilian populations.

Americans, as yet untried by the physical and emotional rigors of widespread destruction, have still the time to prepare themselves; they also have the experience of other countries as a guide to what should be done and what should be avoided. The report referred to above emphasizes preparation of the individual and, through him, of the group to face the conditions envisaged: "What he knows,

thinks, feels and does determines to a large extent what the group will do." Effective leadership and emotional preparedness now, before any attack comes, will go far toward removing the unreasoning dread of atomic bombing per se. Again in the words of the reporter, "The higher the level of general mental health of the community, the more likely it will be to adapt itself to conditions of severe stress."

This period of uneasy "peace" is a time for labor and a time for prayer. Men work to protect themselves and their neighbors against the avoidable panic with its consequent unnecessary death and paralysis of the ability to recover; they pray that the sacrifice of their lives and dearest hopes will not be required of them — and no less that fear, of the known or unknown, will not cause them to be found wanting if the trial and the crisis occur. The alternative to chaos and the shame of defeat is the will to act and thus to survive.

MORE NURSES NEEDED

An eloquent appeal is to be found elsewhere in this issue of the *Journal* from Ann E. Curran, of the Students Health Service of the Boston City Hospital School of Nursing. It is directed to physicians in general, on behalf of a vital auxiliary profession, and contains a specific suggestion — that more physicians should prevail on their own daughters to enter nursing training.

This suggestion is a direct challenge to the medical profession to do its own part in remedying a situation concerning which it constantly complains and yet for which it is in part responsible. For the attitude of physicians toward nurses is one of the inconsistencies of the medical profession. Recognizing the essential necessity of nursing, the high character of service that it requires and the constant numerical shortage of nurses that exists, some physicians will nevertheless patronize and even bully their faithful handmaidens, others will further deplete their ranks by marriage with them, and nearly all will discourage their patients and female relatives from entering training.

The profession of nursing has made tremendous growth in a few decades in the scope and quality of the preparation required for it; in its opportunities for diverse service, as mentioned by Miss Curran, and in its prestige in the community. One of the duties of the physician is to see that its numbers are kept filled with young women capable of assuming its high duties, even if his daughters also must be encouraged to enter its service!

RETIREMENT OF DR. HINTON

On June 30, Dr. William A. Hinton retired from the position that he had held for thirty-six years as chief of the Department of Clinical Laboratories of the Boston Dispensary. He will continue as a consultant at the Boston Dispensary and will retain his position as a director of the Massachusetts Department of Public Health Institute of Laboratories.

To his successor, Dr. Mario Stefanini, Dr. Hinton leaves a tradition long in years and rich in achievement. In his many years of service at the Boston Dispensary, Harvard Medical School and elsewhere, he has won renown for his outstanding contributions to research in rabies and syphilology. His development of the Hinton and Davies-Hinton tests for syphilis remains one of the most significant advances in this special field of medicine. Recognition of his services at Harvard Medical School has already been commented on in these columns.*

Dr. Hinton's record of achievement cannot fail to prove an inspiration to his successor at the Boston Dispensary, as well as to his associates in other institutions. Those to whom his name has become a by-word in his chosen specialty have every confidence that he will continue the research and other activities that have justly earned him a distinction seldom attained in any field.

*Editorial. Distinguished alumnus. *New Eng. J. Med.* 241:34, 1949.

It is said that the Illinois Railroad, from Naples to Jacksonville and Springfield, use castor oil entirely on their car-wheels. The article has done good service in the hands of the faculty, but it will doubtless lose some of its potency should it come to be sold in the market as oil for machinery.

Boston M. & S. J. *August 11, 1852*

MASSACHUSETTS MEDICAL SOCIETY

DEATHS

AHEARNE — Cornelius A. Ahearne, M.D., of Marblehead, died on July 21. He was in his eighty-fifth year.

Dr. Ahearne received his degree from Harvard Medical School in 1889. He was formerly city physician in Salem.

He is survived by his widow, two daughters, two grandchildren, a brother and three sisters.

DOLAN — William E. Dolan, M.D., of Worcester, died on July 21. He was in his seventy-fourth year.

Dr. Dolan received his degree from Baltimore Medical College in 1902. He was a member of the staffs of Memorial and St. Vincent hospitals, and was a member of the New England Ophthalmological Society and New England Oto-Laryngological Society and a fellow of the American Medical Association.

He is survived by a son and a brother.

LENT — Sylvester M. Lent, M.D., of Hinsdale, died on July 21. He was in his forty-seventh year.

Dr. Lent received his degree from Middlesex University School of Medicine in 1937.

He is survived by his widow.

CORRESPONDENCE

TO LIVE IS TO SERVE

To the Editor: For professions that work "hand-in-glove," it seems odd that more doctors do not direct their daughters into the field of professional nursing.

Schools of nursing are now a far cry from those of a few decades ago, being comparable in many ways to a collegiate education. The curriculum today is based on the scientific principles of nursing as well as the skills necessary for a professional nurse.

Whether the student graduates from a diploma school after three years or a degree school after four, basically she has been educated for professional nursing. Certainly, there is no finer profession for any young woman as a career, and certainly there is no profession that offers so many fields of service upon graduation.

Upon completion of even the diploma-school course she has a wide choice of doors to which she holds the key. These include institutional nursing, with its various opportunities, openings in the employ of the Federal Government in highly interesting spots in special fields of nursing such as in Alaska with the Eskimos, on the many reservations for the Indians, and with the Armed Forces in the Air Corps, Army or Navy and, further, if one has the urge to travel, there are the American foreign missions crying for nurses all over the world.

State and local public-health departments offer much to the professional nurse in special divisions, and here the visiting nurse and the school nurse play important parts in community life. To continue, there is the tremendous area covered by the industrial nurse.

After graduation from such a school, nurses will find scholarships available to continue for their degree. With such training they may go into positions as supervisors, instructors, counsellors, professors, deans, principals or directors of schools of nursing — positions that carry dignity, prestige and top responsibilities in the profession.

Here I may emphasize three points for nursing as a career: it is a profession that offers no end of opportunities; it is a profession that offers security; and it is a profession that has rich material rewards — and let me add, it is a profession that combines happily with marriage, for, truly, what finer preparation could there be for marriage than that with a background of nursing education?

So, let one of the nursing profession beg you of the medical profession to guide and direct your daughters into a deeply gratifying career of service, — that of professional nursing.

Have I kindled a spark of interest?

If so, write to:

Committee on Careers in Nursing
2 Park Ave., New York 16, N. Y.

ANN E. CURRAN
Students Health Service
Boston City Hospital School of Nursing
Boston

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BOOKS RECEIVED

The receipt of the following books is acknowledged, and this listing must be regarded as a sufficient return for the courtesy of the sender. Books that appear to be of particular interest will be reviewed as space permits. Additional information in regard to all listed books will be gladly furnished on request.

Case Record from A Sonnetorium. Cartoons by Edward St. J. Gorey. Illustrated with poems by Merrill Moore. Consultants: Louis Untermeyer, Esquire, Professor John C. Ranson, Henry W. Wells, Ph.D., and William C. Williams, M.D. 8°, cloth, 57 pp. New York: Twayne Publishers, 1951. $1.50.

The "Sonnetorium" here mentioned is a cinder block laboratory adjacent to the home of Dr. Moore, where are housed more than one hundred thousand sonnets, written and worked on during his sonnet career. The delightful cartoons by Mr. Gorey depict the trials and tribulations of the sonnet and are supplemented by the verses in sonnet form by Dr. Moore.

Medical Milestones. By Henry J. L. Marriott, M.D. With a foreword by Sir Alexander Fleming. 8°, cloth, 293 pp. Baltimore: The Williams and Wilkins Co., 1952. $3.50.

This book, written for popular consumption, deals with the modern era of the antibiotics, the new treatments for anemia, heart surgery for "blue babies," the antithyroid drugs, hormones and cancer, lepers, leprosy and the public, the Rh factor, rheumatism, cortisone and ACTH, malaria, insects and DDT and seasickness, carsickness and Dramamine. The factual material is authentic and is presented in a nonsensational manner in language easily understood by the laity. The type is large and clear and the printing done on a soft, nonglare paper. The book should be in all public libraries and in the section for popular books in medical libraries.

Any Questions? A selection of questions and answers published in the *British Medical Journal*. First series. 12°, cloth, 240 pp. London: British Medical Association, 1951. 7s. 6d.

In February, 1943, the *British Medical Journal* first presented its column entitled *Any Questions?* The general practitioner soon took to the idea, at first artificially stimulated, and since the beginning there was a steady flow of questions from all parts of the world. There has been a repeated demand for the publication in book form of a selection of the questions. This first series is the direct result of these repeated requests. The material is arranged alphabetically, from allergy to worms, and has been revised by the original authors. There is a good index.

The Battle for Mental Health. By James C. Moloney, M.D. 12°, cloth, 105 pp. New York: Philosophical Library, 1952. $3.50.

This semipopular book considers the subject of mental health in its varying aspects. It includes a description of the Cornelian Corner group and the permissive method as an aid to mental health.

The Dynamics of Psychological Testing: A formulation and guide to independent clinical practice. By Milton S. Gurvitz, Ph.D., chief psychologist, Hillside Hospital, assistant clinical professor of psychology, Adelphi College, and consultant psychologist, Connecticut Commission on Alcoholism. 8°, cloth, 368 pp., with 26 illustrations. New York: Grune and Stratton, Incorporated, 1951. $6.75.

The text of this new book is divided into two main parts: the psychologic procedures (38 pages) and case studies (201 pages). Seventeen cases are discussed and analyzed in a comprehensive manner. They cover the whole field of common mental disorders and aberrations. There is a short list of references and a good index. An appendix comprises a collection of twenty-six line drawings, done by patients.

Roentgen Examinations in Acute Abdominal Diseases. By J. Frimann-Dahl, M.D., Ph.D., chief of Roentgen Department, Ulleval Hospital, Oslo, Norway. 8°, cloth, 323 pp., with 305 illustrations. Springfield, Illinois: Charles C Thomas, 1951. $10.50.

The text of this special monograph is divided into three main parts: normal findings and pathological findings in general and special conditions. There is a chapter by Dr. J. Friedman on the use of the Miller–Abbott tube. The pertinent literature has been examined, and a list of references is appended to the text. There are indexes of authors and subjects. The book should be in collections on diseases of the internal organs and on roentgenographic diagnosis.

Biological Antagonism: The theory of biological relativity. By Gustav J. Martin, Sc.D., research director, National Drug Company, Philadelphia. 8°, cloth, 516 pp., with 64 illustrations and 44 tables. Philadelphia: Blakiston Company, 1951. $8.50.

This book presents a discussion and summary of the present status of the various analogues, proteins, enzymes, vitamins and other biologic antagonists, natural and synthetic. The theory of biologic relativity is defined as the "general law," which underlies all biologic activity and is fundamental in all problems of biology. The text is a mine of pharmacologic knowledge. Bibliographies of selected references are appended to the various chapters and number 1900 items. There is a comprehensive index, and the publishing is well done. The book should be in all medical-library reference collections.

Antibiotic Therapy. By Henry Welch, Ph.D., director, Division of Antibiotics, Food and Drug Administration, Federal Security Agency; and Charles N. Lewis, M.D., medical officer, Division of Antibiotics, Food and Drug Administration. With a foreword by Chester S. Keefer, M.D., Wade Professor of Medicine, Boston University School of Medicine, and chairman, Committee on Medicine and Committee on Chemotherapy of the National Research Council. 8°, cloth, 562 pp. Washington, D. C.: Arundel Press, Incorporated, 1951. $10.00.

The present book brings up to date the knowledge of the use of the antibiotics in the treatment of infectious diseases. The first part of the text is devoted to a description of the various agents and of their activity, pharmacology and dosage, preceded by biographical sketches of their discoverers. There is a chapter on the history of the subject. The second part is devoted to the various types of infections and their treatment. Lists of references are appended to each chapter, and there is a good index. The book is a summary of the subject and should be found useful in the reference collections of medical libraries and to all persons interested in the antibiotics.

Hypertension: A manual for patients with high blood pressure. Revised sixth printing. By Irving H. Page, M.D., director, Research Division, Cleveland Clinic Foundation, Cleveland, Ohio. 12°, cloth, 101 pp., with 7 illustrations. Springfield, Illinois: Charles C Thomas, 1951. $3.00.

This manual was first printed in 1943 and had been reprinted five times by 1947. This sixth printing has been revised, and the subject brought up to date. Half the text is devoted to a discussion of the management of the disease.

NOTICES

ANNOUNCEMENT

Dr. Sidney Kligerman announces the removal of his office to 6 Linnaean Street, Cambridge, on August 25.

ESSEX NORTH DISTRICT MEDICAL SOCIETY

The one hundred and twelfth fall meeting of the Essex North District Medical Society will be held at the Amesbury Country Club, Amesbury, on Wednesday, October 1, at 6:45 p.m.

EXAMINATION FOR PUBLIC HEALTH SERVICE MEDICAL OFFICERS

A competitive examination for appointment of medical officers to the Regular Corps of the United States Public Health Service will be held on October 7, 8 and 9, 1952. Examinations will be held at a number of points throughout the United States, located as centrally as possible in relation to the homes of candidates. Applications must be received *no later than August 26, 1952.*

Application forms and additional information may be obtained from Chief, Division of Commissioned Officers, Public Health Service, Federal Security Agency, Washington 25, D. C.

VAN METER PRIZE AWARD

The American Goiter Association again offers the Van Meter Prize Award of $300 and two honorable mentions for the best essays submitted concerning original work on problems related to the thyroid gland. The award will be made at the annual meeting of the Association, which will be held in Chicago, May 7, 8 and 9, 1953, provided essays of sufficient merit are presented in competition.

The competing essays may cover either clinical or research investigations, should not exceed three thousand words in length and must be presented in English; a typewritten, double-spaced copy in duplicate must be sent to the corresponding secretary, Dr. George C. Shivers, 100 East Saint Vrain Street, Colorado Springs, Colorado, not later than February 15, 1953. The committee reviewing the manuscripts is composed of men well qualified to judge the merits of the competing essays.

A place will be reserved on the program of the annual meeting for the presentation of the Prize Award Essay by the author, if it is possible for him to attend. The essay will be published in the annual *Proceedings* of the Association.

FIVE-YEAR PSYCHIATRIC-RESIDENT PROGRAM IN CALIFORNIA

The California Department of Mental Hygiene offers a five-year psychiatric-resident program with an initial monthly salary of $436 and annual increases to $530 a month in the fifth year. Under this program physicians wishing to qualify for the certificate of the American Board of Psychiatry and Neurology may enter a five-year tour of duty in California's large, modern mental-hospital system. The first, third and fourth years of this term consist of regular psychiatric-residency training. In the second and fifth years, the resident serves as a staff psychiatrist at a California state hospital or clinic.

The psychiatric resident will have the regular California employment benefits of three weeks' paid vacation and eleven paid holidays annually, twelve days cumulative sick leave per year and membership in an unusually liberal retirement system.

Interested physicians or senior medical students should write for the formal bulletin on entrance requirements and application procedure. Inquiries may be sent to the California State Personnel Board, 1015 L Street, Sacramento.

(*Notices concluded on page xi*)